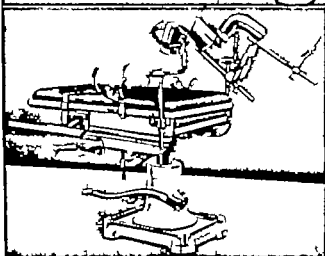
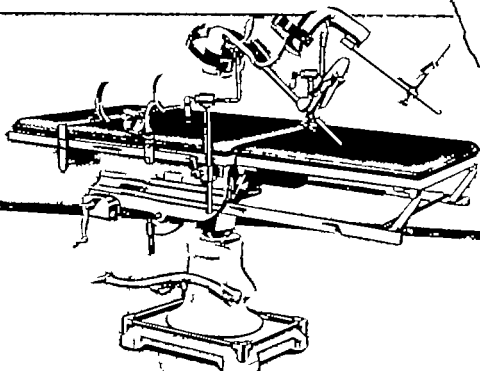


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SURGERY

GYNECOLOGY AND OBSTETRICS

An International Magazine, Published Monthly

VOLUME 80

JANUARY, 1945

NUMBER 1

WAR CASUALTIES FROM PROLONGED EXPOSURE TO WET AND COLD

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OUR experiences with casualties resulting from prolonged exposure to wet and cold during the Attu campaign were reported by one of us (RHP) at the October 1943 meeting in Philadelphia of the Association of Military Surgeons of the United States (5). The cases were classified according to degree of involvement and general principles of treatment were described. The present paper is submitted in order to amplify several features not previously covered to discuss problems emphasized by further study and to report concerning an additional group of cases observed during the past 6 months. Our information has also been supplemented by discussions with medical and other officers who took part in the Attu campaign.

The active phase of this campaign began on May 11 1943, and ended on May 28 1943. For periods varying from 3 to 14 days the soldiers in this operation were exposed to temperatures ranging from slightly above freezing to subzero. Hot food or the opportunity to profit from other artificial or body heat was seldom available. Extremities soon became wet and as a result natural skin oils were lost. The power of supercooling was thus diminished and in the colder areas this probably allowed some true frostbite.

In all cases the cold penetrated deeply into the tissues being aided by the diminished circulation from peripheral vasospasm cramped positions and general muscular inactivity. The ratio of cooling surface to tissue mass as well as the moisture acting as a rapid conductor of heat away from the tissues influenced the distribution and depth of tissue injury. Incidental trauma of walking over rough terrain on the numb feet added to the damage.

While exposure continued there was some swelling of the feet with extravasation of fluids into the tissues small capillary hemorrhages circulatory stasis and beginning thrombosis. After several days when the boots were finally removed the feet were numb like wooden feet, and appeared white or mottled blue and white. Swelling soon increased to a degree that prevented replacement of the boots.

At this time elevation and refrigeration with very gradual warming as advised by Webster Woolhouse and Johnston would have been desirable but battle conditions and the natural desire of the patient to get warm often prompted wrapping and warming of the limb as quickly as possible. The blood vessels which were first spastic (constricted) now dilated the extremity becoming warm and the tissues flooded. Extravasation of plasma and

blood into the already edematous tissues increased as did thrombosis of damaged vessels, circulatory insufficiency and anoxia and tissue necrosis. On superficial tissues blebs formed in some cases were broken and the areas then became infected.

Medical officers and many of the men taking part in the operation commented on the marked variation among different individuals in their susceptibility to wet and cold. Of groups of 3 spending the night in forward listening posts 2 might return with almost no complaint while the third would have numb swollen blue and white mottled feet. This emphasizes the desirability of eliminating beforehand individuals likely to be susceptible to cold such as those with previous foot or leg injuries, those with signs or symptoms indicating vasomotor instability, those with any suggestion of peripheral vascular disease and those with foot infections.

It is of interest that one of the battalions spearheading the attack while suffering battle casualties as high as any battalion in the operation had only 8 of these foot cases requiring evacuation to the rear. This battalion evidently realized the value of preventive meas-

ures, as all of its men had had foot care drills. They had paired off in what they themselves referred to as the buddy system where 2 foot-conscious soldiers worked on each others feet at intervals. Sustained attempts were made to supply the men with an oil or grease to apply to the boots and feet once daily and provision was made when at all possible to relieve each man (especially outposts) for a few hours daily during which time he rested in a relatively dry sleeping bag with the shoes and socks removed and drying.

As these men went to Attu direct from established centers in the United States or Alaska and had not previously been subjected to prolonged dietary insufficiency or to dysenteries, etc. they were a group relatively free from extraneous factors which may influence destruction and healing of tissues. They also were free from constitutional diseases such as arteriosclerosis, cardiorenal disease and diabetes which complicate most cases of gangrene of the extremities seen in civilian practice. The soldiers on Attu had with them but for the most part threw away vitamin C fortified dried lemon juice and medical officers state that a few incipient cases of



Fig. left. The only Japanese prisoner of the Attu campaign received. Letterman General H. J. Tal had gangrenous spots on toes and desquamation on sole of feet.
Fig. right. One of the two Japanese prisoners had had the

right leg amputated. On the left are gangrenous spots, desquamation of skin and the typical foot deformity seen in these cases, plantar flexion of great toe and clawing of small toes.

scurvy were noted before the operation ended. There was probably no relationship between this and the local vascular damage of the extremities in these cases but it might have become an important factor had this campaign lasted much longer.

On admission to Letterman General Hospital pain although generally of only moderate severity was noted in 90 per cent of the cases. Those with gangrene (56 cases) complained of burning pain most severe at night, in the feet and most often in the toes. They also complained occasionally of aching pulling or cramping sensations in the foot or calf muscles. Those without gangrene more often complained of smarting tingling and throbbing mostly of the toes although often of the balls of the feet. Hypesthesia was present in all cases. In general it began at the ankles and increased to complete anesthesia as the toes were approached. Areas of anesthesia were present in all those with gangrene and about a third of those with desquamation only. The degree of anesthesia was usually though not necessarily in proportion to the general severity of the tissue damage. In 2 cases of severe gangrene necessitating amputation of the entire foot, however sensation was comparatively unaltered almost to the line of demarcation while in many showing only a moderate degree of desquamation there was almost com-

plete anesthesia of all the toes. As an indication of the degree of anesthesia, all débride ment and all toe amputations were later done without use of any anesthetic and were painless in almost every case.

Correlation of degree of tissue injury with duration of exposure shows that the length of exposure was not the main determining factor in the severity and extent of tissue damage. This again indicated an individual variation in susceptibility to wet and cold. Thus of the original group of cases received 76 per cent had only desquamation of the skin and no areas of gangrene 14 per cent lost toenails tips of toes and thick layers of the skin (Figs. 1 2 3 4 7 and 8) 10 per cent lost one or both feet or portions thereof such as one or more toes (Figs. 5 6 9 and 10). The average duration of exposure for each of the three groups was about the same 65 days. The least severe averaged 66 days the most severe 64 days. Three patients requiring amputation of both feet were exposed 4 6 and 8 days respectively.

MECHANICAL RESPIRATION AND OXYGEN THERAPY

Twenty-one patients were treated by mechanical respiration produced by alternating positive and negative pressure on the thorax. The mechanical device used was the Terhaar



Fig. 3. Left. Apparent deep gangrene which later was found not to extend as deep as was first believed. (See Fig. 4.)



Fig. 4. Same feet as in Figure 3, 1 month later. Tissue present, only part of nail being lost.



Fig. 5, left. Gangrene of toes, which eventually came to amputation. Compare with Figures 3 and 4 where this damage of toes of left foot was more apparent than real.

Fig. 6 Same feet as in Figure 5, 8 weeks later. Gangrene resulting in loss of toes.

respirator made in two half shells which when clasped together encircle the chest. The rationale for this treatment is as follows:

By increasing the negative pressure in the thorax, there may be induced a change in pres-

sure gradient between that part of the venous and lymphatic bed which lies inside the thorax and that part of the venous and lymphatic tree which is distributed outside the thorax. If true this should result in an increased



Fig. 7 left. Extreme degree of desquamation. Marked cavus and claw foot tendency seen in many of these cases.

Fig. 8 Same feet as in Figure 7 about 4 weeks later. Cavus present. Heavy skin all off. Ulcer left great toe almost healed. Feet tender, balls of feet and toes till anesthetic, 8 weeks after exposure.



Fig. 9. Feet and knees 3 weeks after exposure. Knee ulcers due to crawling, after feet were numb. Feet bluish black boggy moist. Infected zone at line of demarcation. Gas infection developed 5 weeks after exposure (See Fig. 10.)

venous and lymphatic return to the heart, a more efficient cardiac output and in cases such as these an improved capillary flow by the removal of venous stasis and edema.

Mechanical respiration probably differs from the paver boot in the following physiological principles. The boot exercises its negative pressure entirely on the peripheral circulation and may thus increase capillary trauma and extravasation. The chest respirator seems to produce its effect by improving the deep venous and lymphatic return to the heart, thus

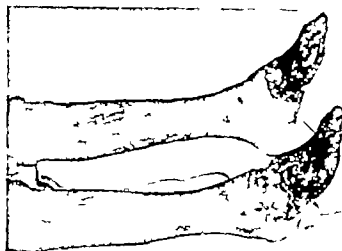


Fig. 10. Same legs as in Figure 9. Foot became mummified but wide soft moist line of demarcation remained (See Fig. 11.)

improving capillary flow by producing a more favorable gradient between the arterioles and venules.

The pressure differentials used were a negative pressure of 10 millimeters of mercury alternating with a positive pressure of 4 millimeters of mercury. This was given at the rate of 18 respirations per minute. Oxygen was administered at the rate of 3.5 liters per minute in a further effort to relieve local tissue anoxia. One hour treatments were given once daily or twice in severe cases.

It was not possible to group the cases in which patients were treated by the respirator and oxygen with comparable control cases with sufficient accuracy to draw a definite conclusion as to end results. There seemed to be however a favorable effect on the lower extremities demonstrated by improvement of color of affected portions and reduction of congestion and edema.

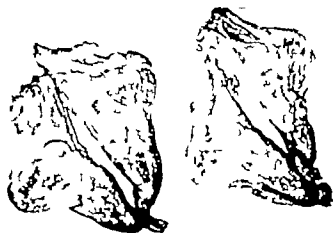


Fig. 11. Same patient as in Figures 9 and 10. Amputated specimens have been sectioned in the sagittal plane. Deep tissue necrosis present.



Fig. 12. Same patient as in Figures 9, 10, and 11. Amputations have been performed 2 weeks before just above ankles, stumps left open, stockinette secured by glue and cut into four strips for traction over pulleys at end of bed. Revision of stumps to be done later if necessary.

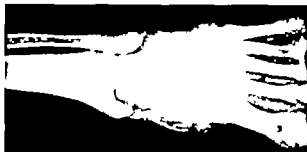


Fig. 3. Gas pockets in soft tissues between metatarsals and medial and lateral aspects of the foot

Despite the favorable local changes here noted it is our opinion that the optimum time for beneficial use of such measures is during the hours and days immediately following the initial trauma. Then the improved venous drainage plus the better tissue oxygenation might be expected to result in an appreciably lessened tissue necrosis.

Although the advisability of some artificial means of improving lymphatic and venous drainage without at the same time increasing local exudation has been previously mentioned (7) it is believed that this represents the first practical application in such cases.

The mechanical respirator and oxygen therapy treatment used on the group of patients discussed was carried out by Captain Robert A. Kennedy, M.C.

GAS INFECTION AND X RAY FINDINGS

In patients with gangrene, cultures taken from the moist demarcating areas at the first dressing at Letterman General Hospital showed a profusion of mixed organisms, including streptococci, staphylococci, *Pseudomonas pyocyaneus*, and members of the colon group. However, infection remained localized to the demarcating zone in all except 1 case.

The patient in this case with gangrene of one foot, complicated by a gunshot wound just above the knee, developed a spreading moist gangrene of the lower leg, accompanied by markedly elevated temperature and pulse. At amputation just below the knee, gas pockets and exudate typical in appearance and odor to that of gas gangrene were found throughout the tissue planes. Anaerobic cultures of the exudate and tissues were negative, while aerobic cultures revealed only *Staphylo-*



Fig. 4. Roentgenogram showing calcium undisturbed in proximal phalanx of gangrenous foot because there was blood supply, whereas marked loss of calcium was present in corresponding bone of opposite foot where blood supply was good.

coccus aureus, nonhemolytic streptococci, *Streptococcus viridans* and *paracolon bacillus*.

In 2 patients with extensive gangrene of both feet, cultures revealed the presence of *Clostridium welchii*. In neither case were there toxic symptoms, and after amputation there was no further evidence of the infection. Dissection of these feet showed both liquefaction and gas formation with positive cultures in superficial and deep tissues. As this occurred 35 days after exposure, it represented a fairly well localized gas bacillus cellulitis, rather than the classical rapidly spreading and highly toxic myositis.

Three other patients with extensive gangrene in whom anaerobic cultures were consistently negative, showed by x ray multiple circumscribed rarefied areas in the soft tissues of the feet (Fig. 13).

The significance of such x ray findings is at times doubtful as separation and retraction of dry gangrenous tissues as well as liquefaction of tissue, will alone or in conjunction with gas-forming organisms, produce similar changes in tissue density. Such changes may also be produced by other organisms such as anaerobic streptococci along with various aerobes, as *Streptococcus pyogenes* and *Staphylococcus*



Fig. 15 Zone of demarcation in one of amputated feet (Fig. 11) Granulation tissue heaped up over epithelial margin and deep inflammatory infiltration amputation 6 weeks after exposure $\times 70$ hematoxylin eosin stain

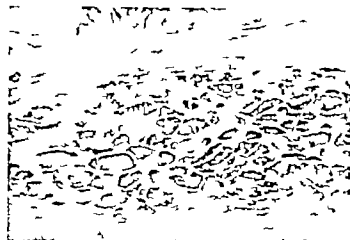


Fig. 16 Skeletal muscle from one of the amputated feet, above zone of demarcation showing atrophy degeneration and a chronic inflammatory reaction Photomicrograph $\times 80$ hematoxylin and eosin stain.

pyogenes (4) One differential point is that changes in tissue density which are due to retraction or liquefaction generally manifest themselves slowly and may vary little from week to week while changes due to gas gangrene may come on more suddenly and spread more rapidly the more severe cases being accompanied by symptoms and signs of toxicity

All patients in whom gas bacillus infection was suspected in addition to sulfa drugs or penicillin or both were given prophylactic x ray treatment of 50 to 100 r twice daily for 3 to 5 days as advised by Kelly and Dowell

The x ray also revealed in most cases a decalcification of nearly all the bones of the feet probably due to immobilization Where complete deep necrosis had taken place and there was loss of blood supply to the tissues, the bones were white and dense little or no calcium being lost (Fig. 14)

VENOUS SYSTEM COMPLICATIONS

One patient who came to midmetatarsal guillotine amputation because of gangrene and cellulitis of the distal half of the right foot developed phlebitis of the greater saphenous vein He was treated with dicumarol and two lumbar sympathetic intracaine blocks and rapid subsidence of the phlebitis resulted

Another patient seen 7 months after exposure had had a phlebotrombosis of the left superficial femoral vein following left inguinal

herniorrhaphy in 1937 Resulting varicose veins were treated by ligation and division of the lesser saphenous trunk in February 1942 Following the exposure on Attu deep phlebotrombosis flared up and was treated by rest and bandages Eight months after exposure there was still moderate aching and swelling of the leg on more than minimal standing or walking Venograms revealed irregularity of the posterior tibial vein no visualization of the superficial femoral vein and development of a narrow tortuous anastomotic channel lying just medial to the femur Incompetent perforating veins carried the blood from the posterior tibial to the greater saphenous vein just below the knee this serving as the main channel of venous return in the thigh This soldier might well have been eliminated from the group prior to invasion of the islands. These were the only two venous system complications of this type occurring in the group

Following second degree involvement cases went on to the Southwest Pacific Slight symptoms increased and 10 and 11 months respectively after exposure these patients were returned to the mainland There was aching pain and cyanosis to just above the ankle on one lower extremity There was no edema. The dorsalis pedis and posterior tibial pulses were weaker than on the opposite side Venograms of both lower extremities were normal This unilateral cyanosis of one foot was more pronounced when the extremity was dependent The condition probably was due

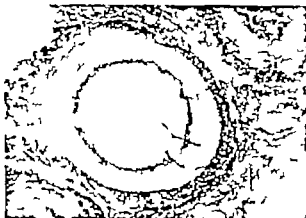


Fig. 7 Posterior tibial artery and veins of amputated foot showing thickened media, and organized, recanalized thrombus 4 cm above zone of demarcation. Photomicrograph $\times 70$; hematoxylin and eosin stain.

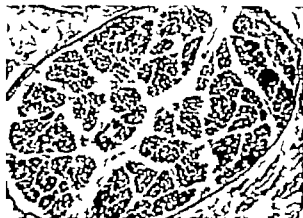


Fig. 8 Microscopic section of nerve of the same foot, 7 centimeters above the zone of demarcation the myelin sheaths are intact. Photomicrograph $\times 5$; Weigert stain.

to local changes in the foot brought on by the exposure

TISSUE DAMAGE AND AMPUTATIONS

Difficulty in distinguishing the severity of the injury identifying viable from nonviable tissue whether due to heat or cold has always been notable and was experienced with these cases. By delay moist gangrene will some times extend but more often what is apparently extensive gangrene may be less extensive than is at first suspected. A black superficial tissue shell may peel off to disclose toes still covered with epithelium (Figs. 3, 4, 7 and 8).

Before amputating most surgeons wait until there is a complete mummification of dead tissues with retraction or separation of the nonviable portions at the line of demarcation. However no patient seen by us progressed to complete mummification all patients retaining a broad moist infected area at the demarcating zone (Figs. 5, 9 and 10).

Amputations of toes or parts of feet for the most part were done on our cases 5 to 9 weeks after exposure and in some cases might well have been done earlier. Such amputations should be done as soon as it is determined that there is no chance of saving the part. Dead tissue left in place harbors organisms, aids in the spread of infection to normal tissues in causes fibrosis and consequent formation of deep scar. Removal of dead tissue is com-

parable with the early removal of deeply necrosed tissue from a burned area, now advised by many as a primary treatment in burns. Any method that will differentiate between viable and nonviable tissues should be used. Dingwall using sodium fluorescein has been able with a fair degree of accuracy to determine a second from a third degree burn. It would be a great step forward if this method should prove of value in cases of varying degrees of gangrene of the extremities.

Amputations of toes should be done just distal to the apparent zone of demarcation. The bones should be cut across as gently as is possible preferably with a small saw and then trimmed with a rongeur to a level a few millimeters above that at which the soft tissues are cut. Care in sectioning the bone will prevent fractures that might aid in the spread of infection. In cases with most marked infection trimming of the bone ends may be left until a week after the soft tissue amputation by which time the infection will have subsided and the danger of osteomyelitis be lessened. A similar open procedure through the midportion of the foot may be performed if it is thought that a satisfactory stump can be obtained.

In cases in which the foot has been damaged severely enough to preclude the probability of success with one of the proved classical foot amputations a sleeve guillotine amputation should be done above the ankle.



Fig. 19. Section of the same nerve as shown in Figure 18 3 centimeters above the zone of demarcation, showing pronounced loss of myelin. Photomicrograph, $\times 225$ Weigert stain.



Fig. 20. Same nerve 1 centimeter above zone of demarcation showing almost complete loss of myelin and proliferation of perineurium epineurium, and endoneurium. Photomicrograph $\times 225$ Weigert stain.

and well above the questionable zone. Later on, a plastic revision or reamputation may be done. Compression bandage and traction on the stump by skin glue and stockinette should be used following the guillotine operation (3). Such stumps usually heal very rapidly (Fig. 12).

Vaseline gauze packs and infrequently changed occlusive dressings over infected or granulating areas are to be condemned for as with the gangrenous parts themselves when left in place drainage is blocked and there is a tendency for the infection to pool or spread.

All granulating areas even the small ones should be prepared for early skin grafting. Normal saline dressings changed two or three times a day have been the most satisfactory means of preparing the granulating area for grafting. Dakin's solution moist penicillin dressings and other preparations have been used in selected cases but have failed to demonstrate any appreciable superiority to saline.

PATHOLOGICAL FINDINGS

Careful dissections were accomplished on the amputated extremities and sections of the larger nerves and blood vessels were taken for microscopic examination from various levels at and above the zone of demarcation.

Below the zone of demarcation the tissues were necrotic and infiltrated with polymorphonuclear leucocytes. At the ulcerated demarcating zone granulation tissue penetrated

quite deeply below the surface (Fig. 15). Above there was a moderate edema and a subsiding spotty organizing inflammatory reaction penetrating along the fascial planes. A loose connective tissue infiltrated with inflammatory cells replaced much of the usual fatty tissue. Muscles showed considerable areas of destruction and replacement with fibrous tissue degenerated muscle bundles being in places scattered throughout a loose fibrous stroma as isolated groups of fibers (Fig. 16).

Examination of arteries and veins at the various levels indicated that some had undergone thrombosis and recanalization others revealed marked acute endothelial proliferation with edema of the walls and focal fibrous thickenings in some there was practically no change (Fig. 17). The vessels were usually thrombosed near the site of demarcation while distal to that level they were necrotic and almost indistinguishable from the other tissues. Thrombosis, even where canalized did not extend more than 3 to 5 centimeters proximal to the demarcating zone. Arteries and veins seemed equally affected.

The nerves at the level of the amputation about 10 centimeters above the zone of demarcation showed the myelin sheaths apparently intact. As the demarcation zone was approached more and more sheaths in each nerve revealed either complete or partial loss with distortion of the myelin. At the



Fig. Eight months after exposure. This deformity was present to some degree in most cases. The great toe pulls downward, small toes upward, and cavus of foot is increased.

actual demarcation zone myelin had completely disappeared as verified by special staining processes. The highest level of demyelination was quite irregular in the various nerves examined (Fig 18 19 and 20)

It must be remembered that these pathological changes were noted in specimens obtained by amputation, averaging about 6 weeks following the initial trauma. No tissues showing pathological changes soon after exposure were available. However the findings in our specimens were those that might be expected to result from the earlier tissue edema, necrosis, and arterial and venous thrombosis, described elsewhere

FOOT DEFORMITIES

A majority of patients seen even including those with only second degree damage developed a foot deformity. This was generally of a claw foot type with varying degree of pes cavus. The great toe was pulled downward into plantar deformity and the intervals between all of the toes were increased (Fig 21)

The mechanism of production of this rather characteristic foot deformity is probably as follows. The muscles of the foot consist of two groups—the long extrinsic ones from the leg and the short intrinsic ones within the foot. There are flexors and extensors in both groups. An intricate balance of all these muscles is necessary for the proper functioning of the foot. It is generally recognized that on prolonged disuse muscle atrophy is more marked

in the intrinsic group than in the extrinsic group. At the time of original exposure chilling and anoxia of all tissues of the feet were probably greater than of the deeper tissues of the leg. This resulted in greater damage to the intrinsic muscles of the feet and their nerve and blood supply than to corresponding structures higher in the leg. Thus the muscles of the foot were first weakened by direct damage and secondarily by atrophy of disuse with a resultant imbalance in favor of the long muscles. The long extensors to the 2nd, 3rd, 4th and 5th toes then pulled the metatarsophalangeal joints into dorsiflexion while the long flexors, uninhibited by the atrophied antagonistic intrinsic muscles, pulled the interphalangeal joints into marked plantar flexion. The flexors to the great toe being stronger than the extensors resulted in a plantar contraction of that toe (Fig 2 4, 7 and 8). The increased interval between the toes was due to the swelling of the tissues, plus the fixation in contraction of the lumbrical and interosseous groups. Some degree of pes cavus is produced by the contracture of the muscular and fascial structures in the plantar aspect of the foot. The appearance of cavus is exaggerated, however by atrophy of the plantar soft tissues and by the plantar deformity of the great toe. This deformity reached its height at around 4 to 6 weeks and then tended to subside partially with lessening of the swelling. A permanent destruction of many muscle fibers no doubt occurs in some of these cases, and thus, together with replacement fibrosis and scarring in the swollen and damaged muscles and fascial planes (see "Pathological Findings") tends to produce permanent weakness and contractures. The importance of the deformities thus produced as primary factors in later disability cannot be overemphasized as they may be very persistent even in second and third degree cases. Of 11 third degree cases (not severe enough to lose toes) observed here 8 to 10 months after the original exposure, 6 had pes cavus and claw toe deformity that evidently contributed materially to deep foot pain on walking. A persistence of marked limitation of dorsiflexion of the great toe due to contracture of the toe flexors was present in 2 of these

These findings call attention to the importance of proper support during the acute phase following injury of the extremities and to early and continued active exercises to prevent or lessen permanent deformity. Exercises should be continued after the patient is ambulatory and arch supports or other types of shoe corrections will be found desirable in many instances. In the late cases (8 or more months after injury) observed by us such foot deformities limited exercise and walking almost as much as the more generally recognized superficial burning pains of the feet. The delay in nerve regeneration in such cases was illustrated by findings of hypesthesia to complete anesthesia of the skin of the toes in all cases. On 2 the hypesthesia extended 3.5 centimeters above the toe webs.

CONCLUSIONS

1. Individuals likely to be susceptible should avoid prolonged exposure to cold and wet and in the case of soldiers the susceptible ones should be eliminated before being moved into such areas.

2. A type of mechanical respirator which seems to improve venous and lymphatic return from the extremities may prove of value especially in the early treatment in such cases.

3. In treating patients with gangrene of the extremities routine periodic, x-ray films and

wound cultures (aerobic and anaerobic) are advised.

4. Tissue retraction and liquefaction in gangrenous soft tissues may produce radiological changes hard to differentiate from those due to gas-forming organisms.

5. These cases do not proceed to the classical mummified dry gangrene types. Amputation should be performed as soon as viable and nonviable tissues can be differentiated.

6. Pathological studies revealed diffuse spotty fibrosis, thrombosis and recanalization of blood vessels, total demyelination of nerves at demarcating zone regressing to normal appearance 10 centimeters above this zone.

7. Characteristic foot deformities and the mechanism of their production are described.

8. Eleven cases 8 to 10 months after injury have been observed.

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SIMPLIFIED DESIGN FOR REPAIR OF SINGLE CLEFT LIPS

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St. Louis, Missouri

SIMPLIFICATION of the design for incisions in repairs of cleft lips may allow more time for concentration on the fundamentals involved in shifting the tissues into position and their fixation and better results may be obtained.

TYPES OF OPERATIONS

I-excision of the cleft and bringing the edges together is the most simple type of repair for single cleft lips (Fig. 1). This plan has been used by many surgeons with good results particularly in partial clefts. One objection to it is the straight line scar which may contract to produce a notch or whistling deformity. Another objection is that the lip which is produced comes straight down (as seen in the profile view) from the nostril floor to the vermillion.

The normal lip curves forward (in profile) just above the vermillion border. This break normally occurs about two-thirds or three-fourths of the way down the lip and a repair which reproduces this kick-out of the vermillion and the skin just above it will more closely resemble a normal lip (Figs. 11 to 18). To do this one needs to use a design which will give an extra amount of tissue in this region and to close the tissues firmly up toward the top of the fornix on the inside.

The Mirault operation a description of which was published over one hundred years ago takes this into account and provides extra tissue at the border by means of a small triangular flap. Mirault used flaps from both the columellar and alar sides of the cleft but his and subsequent experience has shown those from the alar side to be better. This was noted in 1929 by Blair and Brown (1) but the standard flap which was described then was half the length of the lip and this has been found to be too large in some patients.

The main principle of the operation remains just as desirable as ever but better results may be obtained by using a small flap to produce the fullness in only the lower one-third or one fourth of the lip. The simplified plan of marking outlined below (Fig. 1) has been used for 7 years. It has facilitated the entire operation has made the teaching of it easier and has caused some interest to be developed by house surgeons who often appeared bored before.

The essentials of the plan are that (1) A V-excision operation is marked out first (2) then instead of completing this operation a small flap is designed on the cleft side to turn down and across to the central side. This saves tissue fills out the lower border and (when careful mucosal closure is done) leaves a protruding lip.

At the primary operation it is of major importance to obtain (1) a symmetrical alar level (2) a good alar direction toward the columella (3) satisfactory nostril floor (4) a normal nostril curve that is—across the tip (5) a straight columella (6) a full lip border in advance of the lower lip with a normal concavity from above downward (this might be called a flexion crease) (7) a full vermillion without a notched whistling deformity. It is necessary to get primary healing but this is usually not difficult if care is taken in the accurate apposition of raw surfaces and in avoiding tension by the wide mobilization of surrounding facial tissues.

Anesthesia Ether vapor seems to be the safest sedative for babies. If both infraorbital nerves are blocked by injecting 2 per cent novocain around the region of the foramina much less ether will be needed. The vapor is blown through a long curved, sterile metal tube which is held about 1 or 2 inches from the mouth. The anesthetists are encouraged to give just enough so that the baby will remain reasonably still but not enough to

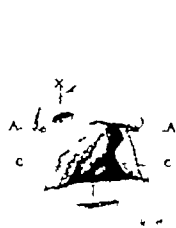


Fig. 1



Fig. 2



Fig. 3

Fig. 1. The V-excision operation. While the columella is held over straight, A is marked at the junction of the skin and vermillion at the level of the base of the columella. X is in the same relation to the columella on the sound side. I bears the same relation to the ala on the cleft side that A bears to the ala on the normal side. C is on the mucocutaneous junction at the point where the vermillion first begins to thin out. C' is on the mucocutaneous junction the same distance from A that C is from I. To do the V-excision operation, A is brought over to A and C' to C after excision of the edges of the cleft.

Fig. 2. The flap operation. The V-excision operation is marked out first. C' is on the mucocutaneous junction at

the most medial point of good full vermillion. B is on the line A-C' equidistant from C' and C. The incision is A-B-C' saving the amount of lip indicated by the shaded isosceles triangle in the insert drawing. B is on the mucocutaneous junction, the same distance from C that B is from C'.

Fig. 3. The lines I-B-C and A-B-C' are lightly incised with a knife. The incision is carried upward from C' on the mucocutaneous junction to separate the vermillion from the skin. This is also done at I to keep any vermillion out of the nostril floor. The circular dotted lines show the area which is to be undermined at the next step.

abolish the cough reflex and it is better to err on the light side. An assistant uses a sucker from time to time to keep the mouth clear of blood. The operator sits above the head of the patient thus seeing the face upside-down throughout the operation. Intratracheal gas ether is used when the patients are old enough (in adults local anesthesia usually suffices).

The marking is done with care after due consideration of all of the elements of deformity in the individual patient. Time spent at this stage will save operative time later because a good design can be followed throughout the operation without change. A mechanical drawing pen and 5 per cent alcoholic methylene blue are used puncturing in the dots, scratching in the lines and wiping off any excess dye with an alcohol sponge.

MARKING OUT THE V EXCISION OPERATION

To mark point A the columellar side of the lip is pushed over into the cleft until the columella is straight and in the midline. I is

then punctured near the mucocutaneous junction on the level of the base of the columella. (It may be put in on this line while it is still in its diagonal position.) Point X is punctured in the floor of the other nostril in a position corresponding to I (Fig. 1).

The relationship of X to the curve around the base of the normal ala is noted. A is then placed in the same relation to the base of the ala on the cleft side. If it is difficult to determine the grooves between the ala and cheek and lip these landmarks can usually be brought out by temporarily pushing the lip medially over into the cleft.

C is on the mucocutaneous line at the medial end of the full thickness of vermillion. This point where the vermillion first begins to thin out can be best ascertained by looking at the lip from above. At times it is almost over to the philtrum on the normal side.

C' is on the mucocutaneous line the same distance from A that C is from I. A small caliper is useful for measuring these distances.



Fig. 4. Incisions made in the buccal fornix on both sides and the soft tissues of the lip and cheek are taken loose from the bone, up almost to the lower border of the orbit on the cleft side. Less extensive mobilization may be necessary on the sound side, though it is sometimes necessary to elevate that nostril up out of the pyriform recess and to cut the base of the septum slightly before the normal ala and columella can be straightened. In any event, the mobilization is continued until the nose can be straightened and the two sides of the lip can be brought together without tension.

(To do the V-excision operation lines are drawn from *A* to *C* and *A'* to *C'* the edges of the cleft are excised accordingly and fitted together.) This operation is not used except in a few partial clefts and in a few secondary operations. It is the easiest design to carry out.

MARKING OUT THE FLAP OPERATION

The V-excision operation is marked out first *C* is then located on the mucocutaneous junction at the highest point where the vermillion on the alar side is still of full thickness. This point where the vermillion first begins to thin out is again most easily seen from above the patient (Fig. 2).

B' is on the line *A-C* and equidistant from *C* and *C'*. The isosceles triangle *C-B'-C'* is the Mirault flap and is the additional amount of lip which is saved by this operation. *B'* is usually about one-third or one-fourth of the way up from *C*.

B is on the mucocutaneous line and the same distance from *C* that *B'* is from *C'*.

Discussion of marking. Any error in placing *A* should be on the low side. The lower the



Fig. 5. Undermining between the lining and skin of the nostril so that they will slide on each other when the nostril is rolled up into a tube. At times it is necessary to make the little vertical cut shown just in front of the turbinate to allow complete rotation of the nostril.

mark the higher the cleft nostril will be and this is the reverse of the common deformity.

An additional check can be had by measuring the distance from *A* vertically down to the mucocutaneous junction. *A-C* should not be greater than this distance or the lip will be too long a common error.

Both *C* and *C'* should be opposite good thick vermillion. This is one of the instances in which two halves cannot be satisfactorily joined to make a whole and if either of these points is opposite thin vermillion a 'whistling' defect is almost certain to result. However if either of the points is placed too far laterally an unnecessary amount of lip will be sacrificed.

Due to the curvature of the surface of the lip one is measuring air distances rather than ground distances in locating all of these points. This would seem to be a source of error but in practice these inequalities usually cancel each other.

THE OPERATION

After one is satisfied with the marking the lines *A-B-C* and *A'-B'-C'* are lightly incised with a knife. The mucosa is also divided from the skin above *A* up in the nostril. The incision on the other side from *C'* is carried upward into the nostril along the mucocutaneous junction. A rectangular skin flap is thus outlined between *C'* and *A* and may be used

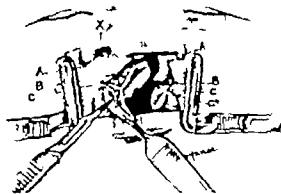


Fig 6 The lightly incised lines $A-B-C$ and $1-B'-C'$ are cut completely through the lip with a stab blade with care to keep knife exactly perpendicular to lip. All angles should be completely opened. The vermilion is inspected and any attached skin removed with a stab blade. The rectangular flap freed from $A-B-C'$ must be loose enough to be rotated up 180 degrees into nostril floor. Dotted lines indicate areas undermined.

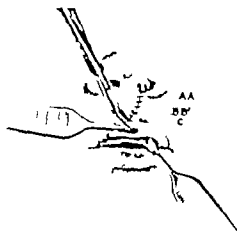


Fig 7 1 and 4 are approximated with a deep stitch of white silk or cotton or No. 000 catgut (knot on the mucosal side) and a surface suture of No. 000 black silk. B and B' are approximated with a fine deep white suture and a black one on the surface. Intervening fine surface sutures are placed and an oblique cut is made in the vermilion flap from C' . For the incisions and trimming fine very sharp scissors are most useful.

later if necessary, to form the nostril floor by rotating it 180 degrees up into place (Fig 3).

Mobilizing the lip and nose. An incision is made in the buccal fornx on the cleft side extending from the molar region forward to the cleft (Fig 4). The soft tissues of the cheek are elevated carefully from the bone up toward the orbital border. This freeing of the

cheek should allow that side of the lip to be brought easily across the cleft and the nostril to be rotated into its proper position. If tightness of the lining of the nose prevents this it may be necessary to make a small vertical incision in front of the anterior end of the inferior turbinate (Fig 5). After the lip and ala are freely mobilized small scissors are

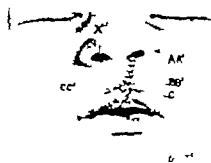


Fig 8

Fig 8 C and C' are united and the vermilion flaps are tented in a zigzag fashion, fitting them so that they lie naturally together without any pull or stretching (Fig 8) then continued on around the vermilion border. The flap in the side to the fornx. The little flap in the nostril trimmed in with the one from the opposite side and they are united together to form the floor. A few key mattress sutures are placed through the ala to unite the lining and covering (which were separated during the undermining).

Fig 9 The mucosal suturing is important and is done with fine interrupted stitches and careful trimming to fit



Fig 9

the edges together. The upper corners are rounded somewhat and the suturing continued to pull some mucosa into the lip from either cheek. This advances the whole lip and thrusts it forward. If the upper edge of the mucosa is tight, vertical lit are made on either side and allowed to spread open.

Fig 10 Normal profile of an infant showing the upper lip far in advance of the lower and the firm crease in the upper lip with the forward thrust of its lower lip. The profile of the upper lip in its relation to the lower lip is visible and not able to be traced. These are some of the finer details of the lip.



Fig 10

introduced through the buccal fornix and the skin of the nose is elevated throughout the lower half and over across the midline toward the normal side (Fig. 5). This tends to minimize corrugation of the lining when the nostril is rotated inward and up to its new position and possibly helps establish a columellar alar angle instead of the straight line that is present here in wide clefts. The undermined cheek is packed temporarily with one-fourth strength adrenalin on gauze.

Similar mobilization of the lip (but not the nose) is done on the opposite side though it is usually not so extensive. If the nose is badly deviated it may be necessary to elevate the base of the normal ala up out of the pyriform recess with a small periosteal elevator. Sometimes it may also be necessary to make a small cut across the base of the septum underneath the lip. When mobilization is complete the two sides of the lip can be brought together with practically no tension.

Excising the cleft. The lines $A-B'-C$ are now cut through the full thickness of the lip care being taken to keep the level of the cut on the mucosal surface identical with the skin. After the incisions have been made any tiny line of skin attached to the vermillion near C should be carefully excised (Fig. 6).

In designing and fitting the two sides together it is better to work with them as though working in wood than as though they were rubber and could be pulled stretched and molded into position. All incisions should be sharp clear cut definitive ones, and when the lip is opened as in swinging the triangular flap down the cut at the angle should be complete so that the angle can fit up snugly against B on the columellar side.

At no time during the whole operation is it desirable to grasp any of the lip which is to be used in the repair with forceps. The gloved fingers are used for most of the holding with a somewhat clumsy appearance but with improved healing and no forcep scratches.

Angled Crie clamps which have a soft spring are used at the corners of the mouth to help control bleeding (Fig. 6). Small mosquito forceps with rubber tubes over the jaws and a rubber band to close them gently may be substituted.

Closing the lip. A and A' are usually closed with a buried No. 000 white silk or cotton suture. If preferred, a large firm No. 000 catgut suture is put in from the mucosal surface picking up a good bit of tissue under both A and A' and thus in one move elevating the ala and closing the lip and nostril in the desired direction (Fig. 7).

B and B' are closed with another fine buried silk or cotton suture and with a fine surface suture. C and C' are fitted together to test the design. An excision is then made so that a V is cut out of the cleft side a vermillion just lateral to C' opening the area and dropping a V shaped flap of the vermillion down. (This is sometimes accomplished by a single appropriate incision simply opening the area, but this gets into the rubber idea and the 'wood working' technique usually is best—Fig. 7.)

On the sound side (after being doubly sure remnants of white skin are off of the vermillion flap below C) the largest sacrifice of tissue is made. The rather long flap of vermillion is fitted across into the open vermillion cut on the cleft side and the excess is cut off. For the incisions and trimming in this region a fine, very sharp scissors is most useful (Figs. 7 and 8).

C and C' are closed with a fine surface stitch. Further surface closures are usually done between AA' , BB' and CC' using fine black silk. The vermillion flaps are closed with fine surface sutures, usually anchoring the points of the flaps first. Mucosal closure is continued by going right on around the vermillion clear up the inside to the buccal fornix and being sure to close the mucosa entirely even if it rests on a raw surface of the premaxilla (Figs. 7, 8 and 9).

This mucosal closure is almost as important as the skin closure. It closes the entire lip for best primary healing and thrusts the lip forward as no other part of the operation does, by being sure there is a free loose amount of tissue below even if the upper end is tighter (Figs. 9 and 10). If this end of the wound seems too tight, it is loosened by vertical mucosal cuts on either side from the fornix downward. This is one of the few places in plastic surgery in which cutting one way and sewing another gives much help. But here the



Fig 11 Repair of wide single cleft lip by method described. The normal-appearing forward thrust of the lower portion

of the lip was obtained by the use of a small flap in the lower one third of the lip with the mucosal suturing.

soft mucosa can actually be transposed in position from a tight pursestring in the fornix to rather free flaps of mucosa that can be advanced into the lip. Complete closure of the mucosa also prevents adhesion of the lip to a raw premaxilla from occurring (Figs 9 and 10).

This point of mucosal closure is dealt with at length because it is the point most responsible for kicking the lip out forward. The fine mucosal sutures put the lip where it can best stay itself. Gross stay sutures may crowd the lip forward but they will not permanently hold the tissue in place. Protrusion of the lip should be accomplished *before* stay sutures are put in.

Stay sutures of B black silk are put in from the mucous surface if desired, going through the lip almost to the skin, usually one or two in number.

The floor of the nose is closed with surface sutures on a small full curved needle, using the flap freed on the columellar side and any part necessary of the flap left from the incision on the cleft side. Care must be taken not to include any vermilion in the floor of the nostril where it could be seen.

The nostril can be somewhat shaped by mattress sutures through it from the skin surface to pick up the mucosa; these two surfaces having been separated during the dissection. One or two are put in the alar fold, one higher up on the ala and one to try to help form an angle at the columellar alar junction. These sutures are not very important and can be omitted (Fig 9).

Many operators use a mattress suture from the alar fold across the floor to tie inside the sound nostril against the septum, using small plates inside and out to prevent cutting of the sutures. If the lip is otherwise solidly closed, one can omit this suture.

The nostril is gently packed with greased gauze and a Logan bow used if desired (Fig 18 b).

At the end of the operation, the lip should be full and in front of the lower (Fig 10). A good flexion crease should be present. The lip should have good width and not be too long. The nostril should have a good floor, the ala should point toward the columella and the level of the ala should be the same or a little higher than the opposite one (Figs 11 to 21).

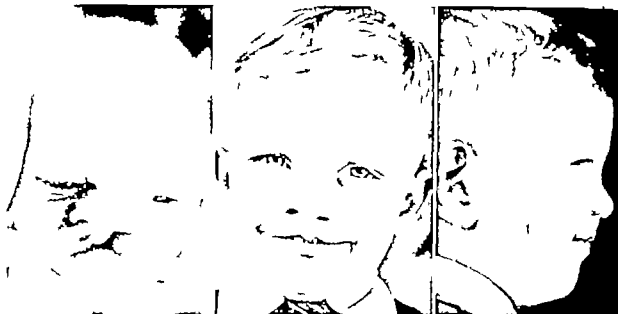


Fig. Wide total single cleft lip. Good nasal symmetry and full, loose lip have been obtained.

PREOPERATIVE DETERMINATIONS AND CARE

Single clefts can be repaired at any time but are preferably closed early in life. An early closure facilitates feeding, eliminates the necessity for constant apologies and explanations to friends by the parents, and the elastic pressure of the closed lip tends to narrow the anterior portion of any associated palate cleft during the first year of life. Even very young babies if they are well developed, tolerate the operation well and closures have been done as early as the age of 7 hours. Quite often the father wishes to have the cleft closed before the mother sees the baby and this may be done but one parent should see the baby beforehand. If the patient is first seen at the age of 3 or 4 days when he is losing weight one might as well wait until he has regained his birth weight before undertaking the repair. The closure should not be done in the presence of jaundice or in prematures or other babies weighing less than 7 pounds until they have attained that weight. Upper respiratory infections are an obvious contraindication as are any pustular skin eruptions but small areas of uninfected miliana or 'heat rash' are not.

None of these children should undergo operation immediately following a trip but they should be under observation for 24 to 48 hours

for rest and to be sure that they have not contracted any upper respiratory infection.

It is still an open question as to whether these patients might not attain better general facial development if the lip and palate closures were delayed until puberty but other factors make this choice untenable. However this is not emergency surgery and should never be done under any except the most favorable conditions. A delay of 1 month will seldom do much harm while a satisfactory repair may be of inestimable value to the child and conversely a faulty repair may cause irreparable damage.

Feeding is always a problem in these infants and especially if the palate is open they are seldom able to nurse from the breast. However it is rarely necessary to gavage them every 3 or 4 hours and an infant's esophagus will usually not stand this procedure long. They can be fed breast milk or a suitable formula with a medicine dropper or a syringe, best given with the baby held almost in a sitting position and taking from 30 to 40 minutes for each feeding rather than the usual 15 to 20 minutes.

POSTOPERATIVE CARE

No dressing is applied over the suture line when good nursing care is available (Fig.



Fig. 13 Several views of a very wide single cleft showing small Blair flap and forward thrust of lower portion of lip. Results shown at ages of 1 and 5 years. The usual

dental deformity is seen. This can be corrected to some extent by orthodontia and limited replacement.

18 b) The nurses are instructed to clean the suture line with alkaline antiseptic solution on tiny gauze pledgets every few minutes for the first hour after operation and then every hour for the remainder of the day. After this the lip is cleansed after each feeding and at other times when necessary to prevent the formation of any clots of blood or serum around the stitches. If experienced nursing care is not available the suture line can be covered with a fine mesh grease gauze dressing which may be changed daily or oftener cleansing the lip each time.

The grease gauze pack in the nostril is removed in 48 hours and the skin sutures on the lip are taken out on the 4th or 5th day. The Logan bow can be removed after 1 week and remaining inside sutures after 10 days.

Feedings are usually given with a syringe until 7 to 10 days after operation after which the baby may nurse from a bottle if the holes in the nipple are burned out and enlarged. If the baby is breast fed the breast milk is usually given with a syringe for 3 or 4 days after operation and then the baby is allowed to nurse if the palate will permit it.



Fig. 4. Extreme deformity with repair showing good lip level and good direction of the ala toward the columella.

The patient is usually discharged from the hospital on the 10th postoperative day with the lip healed, all sutures out, no dressings and able to nurse from a bottle or the breast as far as the lip is concerned.

The co-operation and help of a pediatrician throughout the baby's hospitalization is solicited and gratefully received.

COMMON DEFORMITIES TO AVOID

Deformities can be seen in patients needing secondary repairs (2) and the requirements of the primary operation are thus made more clear. The patients or their parents are apt to focus their attention on the scar, but in many instances this is only a part of the deformity, so that the nose and lip should be studied as a whole piecemeal and in relation to the other features. For surgical correction, secondary deformities are often best evaluated on a footage basis—that is, one that can be seen across the street is worse than one which is only apparent on close inspection.

The tight retruded lip is one of the worst and most common of the cleft lip deformities. Such lips are usually too long vertically and too narrow horizontally and are frequently the result of operating too far out from the cleft and sacrificing an unnecessary amount of substance of the lip. It is usually better to err on the side of having a full wide lip. Even if it is a little short, this tends to improve with growth, and if not, is more amenable to secondary operations. There is practically never any great excess of tissue in a cleft lip, so that the primary excision of the cleft should

involve the least possible amount to get a smooth repair.

Wide star-suture scars are definitely to be avoided as they may never be entirely eliminated. It would be better to risk having the wound open up rather than put wide star sutures on the skin surface.

Notch or whistling deformity of the vermillion. The more common type of whistling deformity is one in which there is a deficient amount of vermillion beneath the lip scar and it is caused by not operating far enough out laterally to get into the full thickness of vermillion on either side of the cleft. Another type is one in which the vermillion may be of almost full thickness beneath the scar but has been pulled up by the contracture of a straight line scar. This can be prevented, in part at least, by the use of a design which will not produce a straight line scar. Some whistling deformities have been both elements of lack of vermillion and scar pull. Excessive shortness of the mucosa may also contribute.

Tight vermillion. The mucocutaneous junction is normally a little out in front of the rest of the upper lip and retrusion or tightness of it is quite noticeable. The use of a small flap, in the operation described here, may help in obtaining a normal forward thrust of the vermillion border. Greatest difficulty may occur in the repair of partial double clefts with the open or lazy W type of notch. This may be due to lack of sufficient vermillion to permit fullness in this region by any design.

Cupid's bow in the vermillion. The slight upward prolongation of the vermillion beneath

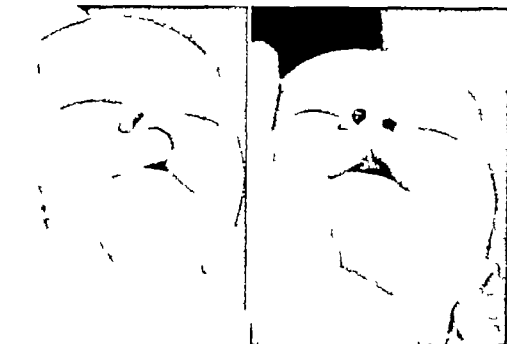


Fig. 15. Extreme soft tissue deformity with nostril on sound side just a slit. This nostril is improved in the repair and the cleft side has a good level, but goes straight into the face instead of toward the columella.



Fig. 16. Same type of deformity as in Figure 15 with skin flap grown down against the open alveolus, so that replacement is difficult. Alar level in the repair is good, but across the tip the alar is not open enough. Lip repair is almost normal in appearance and in muscle action.

the philtrum on either side commonly known as a Cupid's bow is present in some normal lips but almost absent in others. The desire for it among women seems to vary with other fashion trends.

Various operations have been proposed to create it in the cleft lip most of them involving incisions opening up almost the entire mucocutaneous border either at the primary operation or secondarily and substituting a

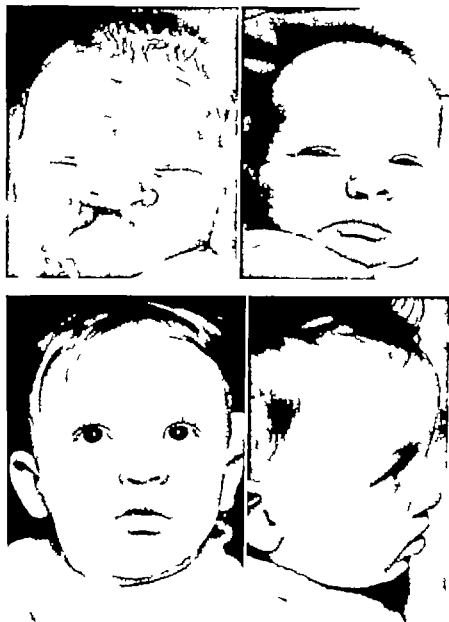


Fig. 7 What is thought to be an excellent repair of an extreme deformity. Second view is just 6 days after operation. Later photographs at _____ years.

long scar for this normal soft undulation of tissue. It is thought that the resultant scar of these operations, in some instances, may be more deforming than the absence of the bow. Men seem to care little for the bow; women are apt to be undecided, and it seems too ephemeral to be the object of an operation in most instances. It can be artificially suggested by very thin areas of tattooing, or in

women by the use of lipstick, without the necessity of putting a permanent scar band clear across the lip.

Disappearing vermillion. Practically no cleft lip deformity is worse than the one with disappearing vermillion, and every effort should be made to avoid it. Of chief importance, is the inside suturing and advancing mucosa forward from each buccal fornix as outlined



Fig. 18. Partial clefts can have all of the problems of complete clefts including those of the nose. This patient has obtained a repair that is good except for the fact that

the thickness of the ala runs vertically into the face instead of starting horizontally to proceed across toward the columella.



Fig. 19. The thickness of the ala in this patient has the proper direction toward the columella. Last view is 1 week after repair

previously. If the mucosa is carefully sutured together clear up to the nasal spine as the last few stitches are put in the lower border of the lip will almost invariably come forward and as it does so the vermillion will roll out. When sutured accurately the inside mucosa will

heal by primary intention and will not become adherent to the raw premaxilla, a common cause of disappearing vermillion. The greatest difficulty is apt to come in partial double clefts with a general deficiency of vermillion.



Fig. 20. The ala on the cleft side has better definition than that on the sound side which itself goes rather straight to the face.

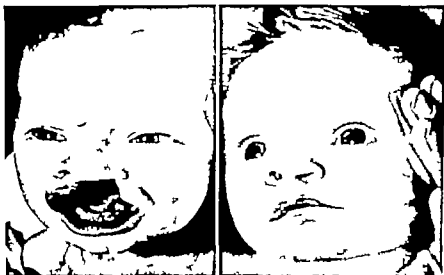


Fig. 21. Extremely on the left, with much more nostril tissue apparent on the left side and extending out as a straight line. Repair shown 5 days after operation. Illustrate rotation of nostril toward columella and lack of nostril along alar border that sometimes occurs when there is too much nostril that rolls up on itself.

Other vermillion deformities Stair-step deformities of the mucocutaneous junction obviously result from inaccurate apposition of skin and mucosal edges. During the later stages of the operation the mucocutaneous junction may be difficult to visualize so that it is quite important to mark this point on

both sides of the cleft before beginning. Redundant vermillion beneath the line of the cleft is the easiest deformity to correct, but the area to be excised has to be carefully determined. Since the opposite deformity (whistling) involves opening the whole lip for correction, it is better to err on the side of

obtaining excess vermillion in this region. Blobs of vermillion may be seen up in the skin of the lip or even in the nostril floor at times and represent gross mistakes in planning or in the operation.

Excessive scar Raised or wide scars in the line of closure may be associated with a true keloidal tendency but are more often the result of other factors. These may be the use of heavy or wide or tightly tied sutures traumatizing the skin edges with forcep marks relying on surface stitches rather than deep ones to hold the lip together closure under excessive tension infection or lack of proper postoperative care to prevent crusting and its sequelae.

Depressed scars may be the result of approximating the skin with the edges slightly turned in or of later slight separation of the skin edges while the deeper structures hold. Scars in any region may tend to become depressed so that as a general principle of wound closure it is probably better to finish a repair with the suture line slightly more elevated than the surrounding tissues. Depression may appear years later in a lip scar in association with an orbicularis muscle deformity.

Tattooing white scars In rare instances an excessively white scar may constitute the chief remaining deformity in the lip of an adolescent or adult. Injection of color directly into the scar with the finest of hand tattooing needles as proposed by Miss Gertrude Hance may be of distinct help. The colors should be light pastel ones and blended together beforehand to match the complexion of the patient. It is often not possible to color the scar uniformly but if one can get enough points of color in to break the visual line of the scar it may no longer be apparent. This coloring will not compensate for raised keloided scars or depressed scars that form shadows in certain lights or other irregularities in the region.

Orbicularis deformity may appear several years after a satisfactory primary repair and it is characterized by thinning of the lip and depression of the scar in the line of closure with lumping up on either side especially on the cleft side. A characteristic bulge in the lip is often seen just beneath the ala on the

cleft side. It is thought to be associated with stretching and thinning of the union between the two sides of the orbicularis muscle as a result of excessively strong or frequent or bicularis movements or weakness in the fibrous union. This deformity may occur clear down in the vermillion due in some instances apparently to a developmental growth or hypertrophy of a small part of the muscle.

Prominent frenulum A large or redundant frenulum may be seen at times in a patient with a cleft lip upon smiling. It may be the result of not taking the mucosa of the lip loose from the alveolus at a low enough level at the time of the original mobilization or to failure of complete mucosal healing from side to side clear up into the fornix.

Lack of nostril floor This deformity may result either from lack of definite planning to construct a floor or to the sacrifice of even a few millimeters of tissue in this region. This is one of the worst deformities to correct and therefore one to be especially avoided at the primary operation.

Slumped nostril In a slumped nostril the ala on the cleft side is usually displaced downward and backward and may be flared outward. Of chief importance in preventing it is rotation of the nostril toward the columella during the primary repair (Figs 14, 19, 20). This requires a good preliminary design and sufficiently wide mobilization of the ala and cheek. It may be necessary to divide the nasal lining between the ala and the end of the lower turbinate to get the nostril far enough forward but incisions that tend to encircle the nostril should be kept to a minimum. It is usually better to set the cleft ala on the same level or a little higher than the opposite one. An associated slanting of the columella may be present if the tissues on the medial side of the cleft have not been sufficiently mobilized during the primary repair. At times this may involve elevating in the pyriform recess to get the opposite nostril up out of the face and freeing the base of the columella underneath the lip in the region of the nasal spine.

Blocked nasal airway on cleft side The most frequent cause is lack of sufficient nasal floor so that the nostril is just collapsed. It

also may result from over rotation of the nostril in the primary repair or from trying to equalize the size of the two nostrils in a very wide cleft. In these latter the actual amount of skin covering and lining may prove to be in excess of that on the normal side when measured. The nostril may extend almost straight out from the columella and trying to roll this excessive amount of tissue into a tube with the same amount of tissue on the small inside diameter as on the larger outside diameter will result in a diminution in the size of the lumen. This is something like trying to roll up a thick piece of sheet rubber to make a tube rather than having it cast as a tube with a small inside and larger outside diameter.

Other nostril irregularities. In a wide cleft the length of the nostril which is rotated to make a tube is longer than on the normal side and the cleft nostril will thus be of larger diameter than the normal one. This could probably be obviated by taking a full thick ~~ness~~ wedge out of the cleft nostril but seems inadvisable in an infant, and there is a tendency for some compensation of this asymmetry during growth. Corrugation of the nostril as it is rolled into a tube is lessened by undermining the skin as outlined. However at times, there may be a remaining single notch or kink in the nostril border usually on the lateral side near the top. This may be due to the fact that the lining cannot slip on the

covering of the nostril right at the rim as it is rotated. In such instances, one can make an incision just inside the rim and parallel to it and by spreading with fine scissors, connect this incision with the previously undermined area. This will usually release the kink and a few carefully placed mattress sutures will help further. The incision should not be too long, as circular scars inside the nostril tend to constrict and form webs and are to be avoided. Figures 14 to 20 represent problems in nasal reconstruction as well as details of the lip itself.

Too large Mirault flaps. A repair with a large Mirault flap (one-half the length of the lip) may be better than a straight line repair but is not so good as when a small flap is used. It is apt to present the following disadvantages (1) the large flaps by their greater contraction are apt to lump up more and give a 'trapdoor flap' effect (2) it is necessary to sacrifice a greater amount of lip on both the cleft and columellar sides to fashion and fit in a large flap (3) the break in the profile line where the forward thrust begins is in the midlip rather than down just about the vermillion border where it normally occurs.

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THE SUPERIORITY OF PENICILLIN OVER BACTERIOPHAGE SULFATHIAZOLE AND CERTAIN OTHER ANTIBACTERIAL SUBSTANCES

As Indicated by Experimental Staphylococcal Infections in Chick Embryos

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THE most important groups of bacteria from the point of view of the surgeon are and always have been the streptococci, the staphylococci and the gram positive sporeforming anaerobes of the gas gangrene group. It is generally recognized that the sulfonamides have taken the terror out of hemolytic streptococcal infections and have reduced the incidence of septicemia from this organism to almost negligible proportions. It was hoped that they would be equally potent against the other two groups but experience has shown that while individual cases may respond promptly and remarkably the great proportion of cases resist sulfonamide treatment.

Our experience during the past 8 years with staphylococcal infections including septicemia has convinced the authors of the value of bacteriophage therapy in this field particularly when clinic and laboratory work together on the problem in hand. The recent availability of penicillin has therefore led us to a study of the relative merits of these two antistaphylococcal agents both with regard to their efficacy in the treatment of staphylococcal infections and their general availability to the profession at large. We have found some clear cut evidence in the experimental data to be presented herewith.

A series of clinical and laboratory experiences with bacteriophage in staphylococcus infections has been reported by us during the last several years (3-8, 10). One of these appeared in SURGERY, GYNECOLOGY AND OB-

STETRICS in 1940 (10) reporting observations made during the 2 year period from 1936 and 1938 in which 21 cases of Staphylococcus septicemia were treated with a mortality of 28 per cent in contrast to a mortality of about 80 per cent in the previous 10 years. While our control series was not run concurrently the results agreed closely with many other reported series. It was found that success depended upon the use of a doubly potent bacteriophage which would not only clear the turbidity of a culture of hemolytic Staphylococcus aureus but would prevent the outgrowth from a transplant from the cleared culture on a blood agar plate.

However the production of doubly potent bacteriophage was attended with considerable difficulty in the laboratory and it was recognized that phage could not be used extensively unless a polyvalent phage of high potency could be produced commercially which would not only be doubly potent against a high percentage of infecting species but which would retain its potency over a long period of time without deterioration. The electron microscopic picture of bacteriophage as shown by Luria suggested quite clearly that phage is a living ultramicroscopic body requiring certain very definite conditions under which it might be expected to survive. Our clinical and laboratory experience with the available commercial phages agreed with reports which were obtained from other sources that they were not dependable.

The search for a method whereby a clear cut appraisal of the value of these two and certain other antistaphylococcal agents might be obtained led us to a consideration of the experimental infection of embryonated hens' eggs

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This research was aided by grant of funds to Columbia University from Lederle & Co., Pearl River, N. Y.

T and M Rakieta were the first to study the action of bacteriophage in developing chick embryos. They used dysentery phages and succeeded in saving the embryos with the bacteriophage given as long as 5 hours following the injection of the bacteria. The majority of the embryos which survived the experimental period of 6 days proved to be free of bacteria and phage was found to have propagated in the medium.

MacNeal Blevins and Pacis using dysentery phage obtained essentially the same results. Green and Birkeland employed the embryonated eggs for the study of the effect of phenol iodine and cetyl pyridinium chloride (ceepryn) on infection produced by *Staphylococcus aureus*. They found that ceepryn had definite curative effects, while phenol and iodine failed.

In addition to bacteriophage and penicillin we have also appraised sulfathiazole ceepryn phemerol, chinazole, antistaphylococcus serum (type A Julianelle of Lederle) and staphylococcus antitoxin (of Lederle).

Among the newly discovered agents we have studied carboxymethoxylamine (CMOA) obtained from Dr E. J. Pulaski of this laboratory viaform (Ciba) and the concentrated extract made from the filtrate produced by a gram positive aerobic sporulating bacillus which has strong antibiotic activity discovered by B. A. Johnson of this laboratory.

TECHNIQUE

Ten day old embryonated eggs were used. The injections of the tested substances were made into the allantoic sac at the edge of the chorioallantoic membrane avoiding the larger vessels. This was done through a small hole made with an egg piercer. In order to relieve pressure within the egg and to allow a free passage of fluid another small hole was drilled into the air sac. After the inoculation both holes were sealed with surgical Scotch tape. The inoculated eggs were kept in the incubators at 38.5 to 39.5 degrees C.

Simultaneously with the egg inoculations analogous inoculations were made into 25 cubic centimeter savita broth tubes, and these were observed for the duration of the egg experiment.

All dead eggs were immediately dissected. The cultures of the egg fluid material and the heart of larger embryos were made on blood agar plates and broth. In a majority of the experiments the eggs which survived the day periods after the inoculation were killed by chilling for 1 hour in the refrigerator and then were dissected and cultured.

In some experiments the eggs were left in the incubator for hatching. The unhealthy chicks which hatched were sacrificed and cultured. The healthy ones were bled from a large peripheral vein for cultures and allowed to grow.

Our experiments were carried out with two strains of *Staphylococcus aureus*. Strain 1 was isolated from a furuncle and strain 2 from the blood stream of a patient.

We found that 0.1 cubic centimeter of a 10 hour savita broth culture of both strains, containing between 150 to 200 million bacteria consistently killed a 10 day old chick embryo within 24 hours. This amount was therefore used as the test dose.

The injections of 0.1 cubic centimeter of 1:10 dilution and 1:100 dilution were also fatal to the embryo died between 1 and 5 days thus making it unsuitable for use as the test dose.

The savita broth cultures were made from blood agar slants which were inoculated directly with the egg material of the culture control egg of the previous experiment.

The bacteriophage employed was our stock staphylococcus mixture. With a titer of 10^8 0.1 cubic centimeter of this phage produced complete visible lysis of 0.1 cubic centimeter of each of two strains of staphylococci when set in 25 cubic centimeters savita broth. (The amount equivalent to the fluid content of an egg.) However a few degenerated colonies often appeared on the blood agar plates, and a viable secondary growth was usually seen after 1 week of incubation. This does not fulfill the criteria of double potency although

doubly potent phage could always be obtained with bacterial inoculations of 0.25 to 0.75 cubic centimeters instead of 0.1 cubic centimeter or when 0.1 cubic centimeter of the 10^8 dilution of phage was added to 0.1 cubic centimeter bacterial inoculum—the optimal concentration for lysis and the propaga-

TABLE I.—THE EFFECT OF STAPHYLOCOCCUS BACTERIOPHAGE ALONE AND IN COMBINATION WITH CEEPRYN AND PHEMEROL AS COMPARED WITH PENICILLIN ON THE CONTROL OF EXPERIMENTAL STAPHYLOCOCCAL INFECTION IN EMBRYONATED EGGS

Substances inoculated	Number of eggs	Death in 24 hours	Cultures		Dead 2-4 days	Culture		Dead 5-7 days	Culture		Lived 7 days or more	Culture		% of eggs survived 7 days or more	% of eggs which were free of growth
			Sterile	Growth		Sterile	Growth		Sterile	Growth		Sterile	Growth		
Culture alone	3	30	—	30	—	—	—	—	—	—	—	—	—	—	—
Culture+phage	9	—	—	—	7	—	7	6	—	5	6	—	5	3	5
Culture+phage+ceepryn	7	—	—	—	6	—	5	5	—	4	6	—	6	35	7
Culture+ceepryn	4	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Culture+phage+pheimerol	3	—	—	—	4	—	3	3	—	3	6	—	5	40	33
Culture+pheimerol	4	—	—	—	3	—	3	—	—	—	—	—	—	—	—
Culture+penicillin	30	—	—	—	—	—	—	4	—	4	5	20	5	64	8

tion of phage being in that ratio of phage corpuscles to bacterial bodies. But such a mixture was not suitable for inoculation into the eggs.

The majority of penicillin experiments were carried out with the calcium salt of penicillin manufactured by Pfizer. This was dissolved in physiological saline in concentrations of 5000 and 1000 units per cubic centimeters and kept frozen in dry ice.

RESULTS

The results with staphylococcus phage. In this series of experiments bacteriophage was injected into most of the eggs immediately following the inoculation of bacteria. Some were inoculated 1 hour after the bacteria.

A group of eggs was also inoculated with bacteriophage and bacteria mixed in the test tube prior to the egg inoculation. Of the 19 eggs, inoculated with bacteriophage immediately following the inoculation of bacteria, no eggs succumbed within 24 hours while the control eggs inoculated with bacteria alone all died. Six eggs lived more than 7 days. Several others survived for 2 to 7 days. Thus the injection of phage immediately after the culture resulted definitely in prolonging the life of the infected chick embryos (Table I).

Almost identical results were obtained in 12 eggs with a mixture of bacteria and bacteriophage made prior to the egg inoculation and in four eggs inoculated 1 hour following the inoculation of bacteria.

Culture of the egg material of all phage treated embryonated eggs yielded with two

exceptions some growth of staphylococci. The amount of growth was always greatly diminished as compared with culture controls. In some cases only a few colonies developed. However, we noticed no consistent correlation between the duration of life of the embryo and the amount of bacterial growth. The signs of phage action on the culture, such as loss of pigmentation of the colonies, fragmentary and degenerated colonies, the presence of phage plaques etc. were always in evidence. Fished colonies which grew in savita were as susceptible to phage as the original culture. The cultures of the egg material as a rule displayed a greater effect of bacteriophage than did the cultures of the blood of the embryos, but it was evident that bacteriophage together with bacteria entered the blood stream of the infected embryo and maintained itself there. Bacteriophage recovered from the egg material of the phage-treated eggs possessed varying degrees of lytic power. In some cases it was able to produce a complete visible lysis of the homologous and of certain heterologous strains of staphylococci. The lytic ability of these phages in savita broth and the degree of colony destruction on the blood agar was always greater than that of the phages which were recovered from the heart of the embryos. Furthermore the titration of egg material in many instances revealed a return of the bacteriophage corpuscular count to the original level and somewhat above this level.

In other cases there were various degrees of diminution of the bacteriophage titer. In a few specimens no phage could be recovered by

the ordinary laboratory methods. Decrease of phage titer and its complete disappearance were especially characteristic of the specimens of egg material stained with blood.

We found no consistent correlation between the potency of bacteriophage isolated from egg material (as estimated by its lytic power and its titer) and the duration of life of the infected embryonated eggs. In order to obtain clearer evidence of the ability of bacteriophage to proliferate in the embryonated eggs, some eggs were inoculated with various dilutions of bacteriophage.

Tenth cubic centimeter amounts of the 10^{-1} 10^{-2} 10^{-3} and 10^{-4} dilutions were used together with susceptible bacteria. The multiplication of bacteriophage was observed with dilutions 10^{-1} and 10^{-2} and not with dilutions 10^{-3} and 10^{-4} . In one of these experiments no multiplication of the phage took place even with dilutions 10^{-2} and 10^{-3} while the undiluted phage decreased in titer. Thus, apparently the chorioallantoic fluid possessed some ability to destroy or neutralize staphylococcus bacteriophage. The degree of destruction varied in different eggs. However if a sufficiently large dose of undiluted phage was used that is 0.1 cubic centimeter multiplication of phage occurred in the majority of cases.

In vitro results with chorioallantoic fluid. In view of the variability in the fate of bacteriophage in different embryonated eggs and the inhibiting effect of the blood of some of the embryos we felt that certain *in vitro* experiments had to be carried out.

For this purpose three specimens of clear chorioallantoic fluid with and without the homologous blood, three specimens of mixed egg fluid with and without blood and three specimens of human serum were used. All specimens were tested undiluted and in dilutions of 1:2 1:10 1:20 1:50 1:100 and 1:200. The titrations of the undiluted and the 1:2 dilutions of each specimen were carried out. We found that complete visible clearing occurred in 1:10 and all higher dilutions of all specimens of chorioallantoic fluid and a partial lysis in undiluted and 1:2 dilutions.

In the presence of blood complete clearing occurred in dilutions of 1:50 or higher with only partial clearing in the lower dilutions.

The titration of the phage in the undiluted and in the 1:2 dilution of chorioallantoic fluid and of the mixed egg fluid material in all but one specimen revealed a definite propagation of bacteriophage to its original level of 10^7 . There was no difference in the titer whether the specimens contained or were free from blood. This titer was equivalent to that of the phage control propagated in savita broth but the titer of phage propagated in the undiluted and in the 1:2 dilution of the human sera decreased 10 to 100 times. Thus, it is apparent that bacteriophage is capable of multiplying and producing lysis of some bacteria in the presence of chorioallantoic fluid and of other fluid constituents of the embryonated egg.

The combined effect of staphylococcus phage with phemerol and ceepryn. From previous *in vitro* experiments with phemerol, ceepryn, zephiran and chinisol, we found that phemerol in a dilution of 1:1 million and ceepryn in a dilution of 1:10 million exerted little or no deleterious effect on staphylococcus phage. At the same time they possessed a significant bacteriocidal effect on staphylococci and other gram positive organisms. It was frequently observed that the combination of phage with phemerol or ceepryn produced a complete destruction of bacterial suspensions, an effect which neither agent could alone produce. We found that zephiran in a dilution of 1:50,000 which was recommended by E. Maier as a bacteriophage preservative definitely cut down the titer and the lytic power of staphylococcus bacteriophage. The same was found true for chinisol (1) widely used as a preservative in Russia.

On the basis of these findings, a series of embryonated eggs were inoculated with staphylococci and treated with ceepryn and phemerol alone and in combination with bacteriophage. The injections were carried out immediately following or 1 hour after the inoculation of bacteria.

The results of the combined treatment are presented in Table I and are essentially the same as those obtained with bacteriophage alone. There was a prolongation of life of the chick embryo, but the majority of the cultures of the egg material revealed sparse phage-contaminated growth. Ceepryn and

TABLE II.—EFFECT OF CALCIUM SALT OF PENICILLIN (PFIZER) ON STAPHYLOCOCCUS INFECTIONS IN EMBRYONATED CHICK EMBRYOS

Number of eggs	Interval between bacteria + penicillin	Dead 3 days	Culture		Dead 4-7 days	Culture		Lived 7 days or more	Culture	
			Sterile	Growth		Sterile	Growth		Sterile	Growth
50	Immediately	4			4		4	3	20	3
8	15 minutes	—	—	—	—	—	—	8	5	2
	1 hour							7	6	
	2 hours			—				7	6	
4	3 hours	—	—	—	—	—	—	4	4	—
6	4 hours	—	—	—	—	—	—	4	4	
4	5 hours	1		—	—	—	—	3		
4	6 hours		1		—	—	—			—
Totals 96			6	6	7		7	67	57	

Survival over 7 day period 70%
Complete sterilization of culture 76%

phemerol alone were less effective (Table I).

The effect of the combined treatment of phage with ceepryn or phemerol given 1 hour following the inoculation was similar to that obtained when these substances were given immediately following the bacterial inoculations.

The injection of 1 per cent chinisol (hydrox yquinoline sulfate) immediately following the inoculation of bacteria produced a sterilizing effect on staphylococci in the egg but it was toxic to the embryos and killed them within 24 hours.

The results with penicillin The injections of different eggs were made at varying intervals following the inoculation of bacteria. Some eggs received penicillin immediately after the bacteria others after 15 minutes 1 hour 2 hours 3 hours, 4 hours 5 hours, and some 6 hours following the bacteria. Doses of 0.1 cubic centimeter of penicillin containing 500 units, 100 units, 10 units, and 1 unit were used.

The results of the experiments on the effect of the calcium salt of penicillin of Pfizer is presented in Table II. From this chart one can see that 96 embryonated eggs were injected with 100 units of penicillin immediately and up to 6 hours following the inoculation of bacteria. Sixty seven of these 96 eggs, that is 69 per cent survived a 7 day experimental period. Of these 57, or 85 per cent did not yield any growth on the culture. Sixteen more eggs of the 29 which died within the experimental period were found free of growth. The

cultures of the eggs inoculated with penicillin were made in plain broth and on blood agar plates in the presence of clarase (9).

In those instances in which the growth of staphylococci persisted it was rarely as abundant as in the culture controls and the colonies looked degenerated. There was no significant difference in the outcome of the penicillin therapy when it was given immediately following the inoculation of bacteria or within a 6 hour period. These experiments must be repeated with still longer intervals up to 24 hours.

Thus the injection of 100 units of penicillin exerted a definite protective effect on the infected chick embryos. It was often capable of destroying all of the inoculated bacteria. And even in those eggs in which the sterilization was incomplete penicillin prolonged the life of the chick embryos. It also allowed hatching of some of the eggs, which were incubated over the 7 day experimental period.

Table III shows the therapeutic and sterilizing effect of 100 units, 10 units, and of 1 unit of penicillin. In this experiment the injections of penicillin were made immediately following the inoculation of bacteria or within a 4 hour period. Once again there was no significant difference in the protective power when 100 units or 10 units of penicillin were given but the protective power of 1 unit was lower. However there was a marked difference in the bactericidal effect of different amounts of penicillin when cultures were made 100 units

TABLE III.—COMPARATIVE THERAPEUTIC EFFECT OF 100 UNITS, 10 UNITS AND OF 1 UNIT OF PENICILLIN (CALCIUM SALT-PETZER) ADMINISTERED IMMEDIATELY AFTER 1 HOUR, 2 HOURS AND 4 HOURS FOLLOWING THE ADMINISTRATION OF BACTERIA

Number of units	Interval between bacteria & penicillin	Number of eggs	Dead 3 days	Culture		Dead 4-7 days	Culture		Lived 7 days or more	Culture			
				Sterile	Growth		Sterile	Growth		Sterile	Growth		
100	Immediate	—	—	—	—	—	—	—	—	—	—		
	1 hour	—	—	—	—	—	—	—	—	—	—		
	2 hours	—	—	—	—	—	—	—	—	—	—		
10	Immediate	—	—	—	—	—	—	—	—	—	—		
	1 hour	—	—	—	—	—	—	—	—	—	—		
	2 hours	—	—	—	—	—	—	—	—	—	—		
1	Immediate	—	—	—	—	—	—	—	—	—	—		
	1 hour	—	—	—	—	—	—	—	—	—	—		
	2 hours	—	—	—	—	—	—	—	—	—	—		
100	1 hour	—	—	—	—	—	—	—	7	—	—		
	2 hours	—	—	—	—	—	—	—	—	—	—		
	4 hours	—	—	—	—	—	—	—	—	—	—		
10	1 hour	—	—	—	—	—	—	—	—	—	—		
	2 hours	—	—	—	—	—	—	—	—	—	—		
	4 hours	—	—	—	—	—	—	—	—	—	—		
1	1 hour	—	—	—	—	—	—	—	—	—	—		
	2 hours	—	—	—	—	—	—	—	—	—	—		
	4 hours	—	—	—	—	—	—	—	—	—	—		
100	1 hour	6	—	—	—	—	—	—	—	—	—	6	6
	2 hours	—	—	—	—	—	—	—	—	—	—	—	—
	4 hours	—	—	—	—	—	—	—	—	—	—	—	—
10	1 hour	—	—	—	—	—	—	—	—	—	—	—	—
	2 hours	—	—	—	—	—	—	—	—	—	—	—	—
	4 hours	—	—	—	—	—	—	—	—	—	—	—	—
1	1 hour	—	—	—	—	—	—	—	—	—	—	—	—
	2 hours	—	—	—	—	—	—	—	—	—	—	—	—
	4 hours	—	—	—	—	—	—	—	—	—	—	—	—
100	Total	6	0	—	—	—	—	—	—	—	—	6	6
	Total	—	—	—	—	—	—	—	—	—	—	—	—
	Total	—	—	—	—	—	—	—	—	—	—	—	—

of penicillin sterilized 19 out of 32 eggs, 68 per cent 10 units of penicillin sterilized only 8 out of 22 eggs, 36 per cent 1 unit of penicillin failed to sterilize a single egg that lived longer than the 7 day experimental period.

Analogous experiments carried out with 100 units, 10 units and 1 unit of penicillin in 25 cubic centimeters of savita broth revealed the following. Both 100 units and 10 units of penicillin produced a very marked bactericidal effect on staphylococci and frequently produced the destruction of all bacteria. In some experiments however a few bacteria survived the whole 7 to 12 day period of incubation. During this time the savita broth remained clear and the presence of bacteria could be revealed only by inoculating blood agar plates. One unit of penicillin also possessed a significant bactericidal power in the savita broth which was clear after 24 hours of incubation but it usually showed growth after 72 hours of incubation.

The injection of 500 units of penicillin proved to be toxic for some of the eggs. And although 3 out of 9 eggs survived for 6 or more days, 6 others, including 3 controls, inoculated with penicillin alone perished within 2 days.

OTHER BACTERIOSTATIC AGENTS

Sulfathiazole (ST) was used in a concentration of 185 milligrams per cent (the highest concentration possible in water). One-tenth to two-tenths cubic centimeter of the drug were administered immediately following the injection of staphylococci. No significant beneficial effect was observed as all chick embryos died within 4 days. The culture of the egg material showed some diminution and a marked degeneration of the bacterial growth. Similar results were obtained with the combined administration of bacteriophage and sulfathiazole in 6 infected eggs. Among 3 control eggs, inoculated with 0.2 cubic centimeter of sulfathiazole alone 2 died within 3 days, while 1 lived for 5 days.

Thus the results seem to indicate the lack of beneficial effect and an apparent toxicity with this concentration of the drug in the chick embryo.

The experiment *in vitro* demonstrated that 0.25 cubic centimeter of a solution containing 57 mgm of ST produced only a slight inhibitory effect against a culture (150-200 million bacteria) in 25 cubic centimeters of bacteriophage savita broth. The inhibition was complete when a small number between 15,000 to 100,000 bacteria were present.

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Both substances produced some prolongation in the life of the embryos but none lived longer than 7 days.

Cultures of the egg material of the serum treated eggs did not reveal any significant diminution in the amount of growth as compared with the culture controls and there was no apparent degeneration of the colonies.

Both types of sera exerted a slight inhibiting effect *in vitro*.

Carboxymethoxylamine (CMO 1) immediately following the inoculation of bacteria resulted in a slight prolongation of life of the embryos. The drug also produced a complete destruction of all bacteria in some of the infected eggs. However it was obviously toxic having killed all the 4 control eggs within 2 days. It was interesting to note that having possessed a considerable bactericidal effect CMOA did not reduce the titer of bacteriophage or interfere with its proliferation when used concurrently. The marked bactericidal effect of CMOA and its harmlessness for bacteriophage were confirmed *in vitro*.

Vioform (Ciba) was employed in concentrations ranging between 1:200 and 1:500,000 or 1 cubic centimeter of these dilutions being administered immediately after the bacteria. No protective or bacteriostatic effect was observed with this agent *in vivo* and there was no significant inhibiting action *in vitro*. In concentration of 1:200 vioform was not toxic for the embryos.

B. A. Johnson's Bacillus T (antibiotic) The filtrate from a 3 day culture of this organism in various media is nontoxic for animals and has a strong bacteriostatic action *in vitro* against all of the gram positive organisms with which it has been tested. It may be concentrated by a number of methods which will be reported elsewhere. The substance used in these experiments was a crude concentrate containing about 100 units per cubic centimeter. It proved to be efficacious in prolonging the life of the embryos but was not as good as penicillin. Three out of 4 injected eggs survived the 7 day experimental period and one of these hatched. However the cultures showed only a partial inhibition of the growth and there was invasion of the blood stream.

The chick which hatched revealed the presence of bacteria in the absorbed yolk sac—but there was no invasion of the blood stream.

SUMMARY

1 The inoculation of the chorioallantoic fluid of 10 day old chick embryos with 0.1 of a savita broth culture of *Staphylococcus aureus* consistently brought about the death of the embryos within 24 hours.

2 The administration of staphylococcus bacteriophage immediately following the inoculation of bacteria prolonged the life of all chick embryos.

3 The cultures of the egg material of the phage treated embryonated eggs resulted in a

decrease and a degeneration of bacterial growth. However a complete sterilization was seldom achieved.

4 The presence of bacteriophage in the chorioallantoic fluid usually did not prevent the bacterial invasion of the blood stream of the embryos although the appearance of phage in the blood usually could be demonstrated.

5 Active multiplication of bacteriophage occurred in the majority of the cases when the undiluted or lower dilutions of phage were used. But dilutions of 10^{-4} or higher seldom multiplied and often completely disappeared.

6 The *in vitro* experiments carried out with chorioallantoic fluid and with a mixture of the egg material showed that staphylococcus phage not only multiplied in these fluids but also produced a lysis of susceptible bacteria suspended in them. The presence of embryonic blood did not prevent bacterial lysis although there was some inhibition.

7 The addition of ceepryn or phemerol did not significantly change the therapeutic results of bacteriophage treatment of the infected embryonated eggs.

8 The administration of 100 units of the calcium salt of penicillin anytime within 6 hours following the bacterial inoculation resulted in survival of the majority of the embryonated eggs for the 7 day experimental period and in hatching of eggs when incubation was prolonged beyond this period.

9 The therapeutic results were essentially the same when 10 units of penicillin was administered but survivals fell off when 1 unit was used.

10 The sterilization of the infected eggs however depended upon the numbers of units of penicillin used. A complete sterilization occurred in 76 per cent of all eggs inoculated with 100 units of penicillin.

11 The administration of 28.5 or 57 milli-grams of sulfathiazole simultaneously with the bacteria failed to prolong the life of the embryonated eggs or to produce significant bacterial inhibition of the test dose.

12 Antistaphylococcus rabbit serum (Julianelle) and staphylococcus antitoxin horse serum in 0.1 and 0.2 cubic centimeter amounts produced some prolongation of the life of the

eggs but the antibacterial effect of these substances was also insignificant

13 Carboxymethoxylamine (CMA) tested in 0.5 per cent concentration produced a sterilizing effect *in vivo* and *in vitro* in a majority of the cases but was found toxic for the embryos. Only the local use of this drug can be considered safe

14 Vioform in 0.5 per cent concentration was not toxic but possessed only a slight bacteriostatic effect

15 The new antibiotic agent discovered by Miss B. Johnson from *Bacillus T* a gram positive sporulating bacillus, exerted a significant protective effect of the embryos but in the concentrations which were used it was not as efficient as penicillin

CONCLUSIONS

1 Penicillin is outstanding in saving chick embryos or prolonging life when inoculated with virulent hemolytic *Staphylococcus aureus* cultures in doses which regularly kill controls in 24 hours. In this respect it is superior to staphylococcus bacteriophage or staphylococcus antitoxin or vioform or carboxymethoxylamine or sulfathiazole or another antibiotic derived from *Bacillus T*

2 The increasing availability of penicillin and its demonstrated efficiency in the clinical treatment of staphylococcus infections relegates the use of staphylococcus bacteriophage in these infections to a place of second rank and only to be considered in cases in which penicillin fails.

3 Our efforts to produce a more highly potent staphylococcus phage by the use of egg embryos has not been successful. The difficulties of developing a commercial phage of high potency and prolonged activity still remain

4 Further studies are indicated in the field of antibiotics for the staphylococcus and other organisms

5 Egg embryos offer a reliable medium for the appraisal of antistaphylococcus agents and other antibacterial substances.

During the writing of the present publication, a paper by Green and Burkland has appeared in the *Journal of Infectious Diseases* 94, 74. Among various wound antiseptics the authors studied the effect of penicillin, crepryn and phenmerol. The results obtained by these authors with penicillin are similar to ours. Crepryn and phenmerol were used in much higher concentrations and were found to be effective sterilizing agents

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EXPERIMENTAL STUDIES OF PERIPHERAL NERVE INJURIES

III A Study of Recovery of Function Following Repair by End to End Sutures and Nerve Grafts

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A STUDY was made of the recovery of function following section of peripheral nerves by a razor blade and gunshots and repair by end-to-end sutures and nerve grafts

The experiments were performed upon 470 cats and the nerve involved was the sciatic. Procedures were standardized so that two surgeons performed all the operations and followed the same methods and technique. Identical methods of clinical examination were used by two examiners.

OPERATIVE PROCEDURES

Following induction by intravenous nembutal anesthesia (nembutal gr 0.2 per pound of weight) the animal was tied to a board with the hind legs in extension at the hips and slightly flexed at the knees. The external aspect of the left thigh was shaved, the skin prepared with iodine and alcohol and draped. The entire operative procedure was done under strict asepsis. A 6 centimeter long incision was made parallel to the femur on the posterior surface of the thigh its upper end reaching a point half way between the tuberosity of the ischium and the greater trochanter. The skin and subcutaneous tissue were retracted and the line of cleavage between the biceps femoris and the vastus lateralis muscles was exposed. These muscles were retracted from each other thus exposing the caudo-femoral the lower border of the gluteus maximus the lateral surfaces of the abductor femoris and semimembranosus muscles the fat

of the popliteal space and the sciatic nerve in its entire course in the thigh from the level where it gives off branches to the hamstring muscles to a point below its division into the tibial and common peroneal nerves. The length of nerve exposed averaged 6 centimeters. Section of the nerve with a razor blade and repair were performed in its proximal half.

A detailed description of the technique used to obtain uniform experimental gunshot nerve injuries was given in a previous article.

A SHARP SECTION EXPERIMENTS

End-to-end sutures were performed in 34 animals. After exposure the sciatic nerve was lifted from its bed and sectioned with a razor blade at a point about 3 centimeters above its division or 1 centimeter from the point where it usually disappears beneath the caudofemoral muscle. The sectioned ends of the nerve were accurately approximated by five to six sutures uniting their epineurial sheaths. The sutures employed were a single untwisted strand of black twisted Champion surgeon's silk No. 4. The nerve was not sutured until all epineurial and perineurial bleeding had stopped and special care was taken to suture only the epineurium. The nerve bed was kept moist with saline solution during the operation. The fascia of the biceps femoris and vastus lateralis muscles was approximated with one or two silk sutures and the skin was closed with clips. The wounds healed without infection and the clips were removed on the 10th postoperative day. No dressings were applied and the leg was not immobilized.

Autogenous grafts were performed in 85 animals. A piece of the exposed sciatic nerve measuring from 2.0 to 2.5 centimeters was re-

From the Division of Surgery, Northwestern University Medical School. The work described in this paper was done under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Northwestern University.

sected and resutured into its previous position without taking special care in the approximation of the cross section fascicular pattern of the nerve. The graft was frequently rotated. Five to six silk sutures approximated the epineurium of the graft to the epineurium of the proximal and distal nerve segments. The distal suture line was situated approximately 1.5 centimeters above the division of the sciatic nerve.

Homogenous grafts were performed in 71 animals. The graft measuring from 2.0 to 2.5 centimeters, was taken from the sciatic nerve of another cat and sutured into a gap produced by the resection of a nerve segment of equal length. The ends of the graft were approximated by 5 to 6 epineural sutures to the proximal and distal nerve segments without paying particular attention to the cross section fascicular arrangements of the nerve. The homogenous grafts were usually transplanted immediately after they were obtained; in a few cases they were kept in sterile saline solution for 24 hours and in 8 animals the grafts were preserved for various periods in 2 per cent, 50 per cent and 70 per cent alcohol before transplantation.

Following end-to-end suture the repaired nerves were removed after a period of 30, 45 or 60 days. In a large number of autogenous and homogenous grafts the distal suture line was resected for a length of 0.5 to 1.0 centimeter depending upon the amount of scar and the mass of neuroma present 45, 60 or 75 days after implantation of the graft and a new distal suture was performed. The repaired nerve was removed another 45, 60 or 75 days later or 90, 120 and 150 days after primary implantation of the graft.

At autopsy the entire sciatic nerve was removed including its tibial and peroneal divisions as far as the ankle. The specimen was suspended on glass rods and fixed in a 10 per cent formalin solution and imbedded in paraffin. Serial longitudinal and cross sections of the specimen above and below the point of repair and of the graft were stained to show the connective tissue, myelin sheaths and nerve fibers according to the van Gieson, Weil, Bodian, Sudan III, silver pyridine and Bodian fuchsin methods.

ANATOMICAL APPEARANCE OF THE REPAIRED NERVES

a End-to-end sutures. The gross appearance of the nerve and suture lines was about the same 30, 45 and 60 days after repair. In most of them a few thin adhesions were present between the suture line and the surrounding tissue in which numerous small blood vessels could be seen. The adhesions were never severe enough to immobilize the nerve or to fix it to one of the surrounding muscles. Usually a slight swelling was observed at the suture line on which the black silk sutures could be seen (Fig. 1).

b Autogenous grafts. The grafts usually appeared to be thicker and more voluminous at the time of removal than at the time of implantation and were also thicker than the proximal and distal nerve segments to which they were sutured. The proximal suture line was usually slightly swollen and the distal suture line showed in most cases a medium amount of swelling 45, 60 and 75 days after implantation of the graft. This swelling of the second distal suture line seemed to be smaller an equal number of days after the primary distal suture line had been resected and resutured. Well formed blood vessels could always be observed in the epineurium of the graft penetrating the epineurium at the distal suture line and traveling toward the proximal suture line. A small amount of thin adhesions were also present around the suture lines and the graft but generally did not immobilize the nerve. These adhesions carried numerous blood vessels including those which were seen in the epineurium (Fig. 2).

Homogenous grafts. The anatomical appearance of these grafts differed from that of the autogenous grafts in so far as they were thicker, more voluminous, had a fusiform shape and gave the macroscopic impression of a neuromatous mass (Fig. 3). Both suture lines were swollen, the distal more than the proximal. Larger amounts of adhesions surrounded the graft and connected it with the surrounding tissues and frequently small muscle bundles were attached to the thickened epineurium and immobilized the graft. The adhesions were always very vascular and numerous blood vessels could be seen entering

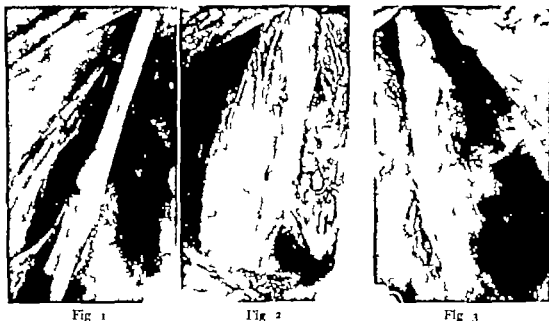


Fig. 1 Sixty days after end-to-end suture of the left sciatic nerve. There is a slight swelling of the suture line but no apparent adhesions between the nerve and the surrounding tissue.

Fig. 2 Autogenous graft 120 days after transplantation into the left sciatic nerve. A slight swelling of both suture lines is present; silk sutures are visible at the site of the distal suture. There are a few adhesions between the graft and the surrounding tissue. Small blood vessels can be seen in the epineurium of the graft.

Fig. 3 Homogenous graft 75 days after transplantation into the left sciatic nerve. The graft is spindle shaped and thicker than the proximal and distal nerve segments. The swelling of the suture line is more marked distally. Strands of adhesions are present between the graft, the suture lines and the surrounding muscles.

the epineurium of the graft. When the graft was freed from its adhesions the surface of the thickened epineurium was usually covered with minute drops of blood. In a few cases in which a large swelling of the proximal suture line was always present the graft remained thin, had a fibrotic appearance and a hard and stringy consistency, and the distal suture line was only slightly swollen.

A few alcohol stored homogenous grafts have been used and they differed from the other fresh homogenous grafts by their pale and more fibrotic appearance and only a few small scattered vessels were present in the epineurium. They were also surrounded by poorly vascularized adhesions and the suture lines were equally swollen.

After resection and resuture of the distal suture line new adhesions formed between the suture line and the surrounding tissue. The secondary suture line was generally smaller than the resected one but some swelling was always present. In animals which were allowed to live for longer periods of time up to 33 months the grafts appeared to be of the

same size as the proximal and distal nerve segments and the suture lines were often indistinguishable from the graft and the rest of the nerve. The adhesions were usually very thin and the graft as a whole did not differ from a normal nerve. This was particularly true of the autogenous grafts. The epineurium of the homogenous grafts was never as smooth and transparent as that of the autogenous grafts or the normal nerves.

MICROSCOPIC STUDIES

Depending on the age of the specimen the serially sectioned and stained nerve and graft specimens showed various signs of degeneration and regeneration.

Although the nerves were sectioned with a sharp razor blade and repaired by delicate suturing of the epineurial sheaths with fine silk, the site of section and repair always showed a traumatic zone within a few millimeters of the two ends. This area was characterized by a breaking down of the myelin edema and an accumulation of debris between the endoneurial tubes in place of the



Fig. 4. Distal segment of the left sciatic nerve 30 days after end-to-end suture. The endoneurial tubes are filled with myelin decomposition products and large number of xitter cells is present especially around the capillaries. Regenerating nerve fibers follow the endoneurium which shows a cellular proliferation (Bodian fuchsin stain $\times 70$).

original myelin sheaths. The axon cylinders also underwent degenerative changes and finally broke down completely. The trauma led within a few days to a proliferative reaction of the endoneurium in the end of the proximal segment, which resulted in structural obliteration of the original endoneurial tubes and was accompanied by disturbances in the removal of the myelin decomposition product. Regeneration took place almost immediately and was first observed as a proliferation of the Schwann cells and by an unravelling of the axons into numerous fibrils. Regenerating nerve fibers were present 5 days after suture within the original endoneurial tubes in the proximal segment frequently accompanying old axon cylinders and always attached to proliferating Schwann cells. In the traumatic zone where the irregular proliferation of the endoneurial mesodermal cells had changed the original nerve structure and where traumatic myelin products were present numerous Peroncito spirals were found.

Mesodermal and ectodermal cellular proliferation followed by the formation of numerous capillaries took place simultaneously in the distal segment of the nerves repaired by end-to-end suture. Regenerating nerve fibers entered the suture line following the path of proliferating histiocytes in the granulation tissue during the first week after suture. They were closely attached to the proliferating cells

and were accompanied by newly formed fine collagenous fibers. Beyond the small traumatic zone in the distal segment the regenerating nerve fibers were seen in close contact with the cellular endoneurium and the Schwann cells in the outer zone of the endoneurial tubes which were filled with decomposed myelin and the fat globules characteristic of Wallerian degeneration. From one axon a large number of fine fibrils might sprout and fan out in all directions into the suture line along the scaffolding laid down by the proliferating mesodermal cells.

The trauma also caused a reactive epineurial proliferation which had the characteristics of a symptomatic inflammation. This proliferation took place on the surface of the proximal and distal segments as a continuation of the mesodermal reaction of the suture line. The epineurial reaction lost its chronic inflammatory character and decreased gradually as time went on. Some of the regenerating nerve fibers, fanning out at the suture line, followed the proliferating mesodermal elements outside the limits of the nerve into the proliferating epineurium and perineurium. These deviating epineurial nerve fibers have been observed over the distal segment and also over the proximal segment where they took a retrograde course and often penetrated deep into



Fig. 5. A togenous graft 30 days after transplantation showing a monomorphous structure and neurotization similar to that of regenerating peripheral nerve. The old endoneurium is preserved and directs the band and nerve fiber proliferation. Remaining myelin decomposition products show the arrangement of the original endoneurial tubes characteristic of degenerating nerve. The borderline between perineurium and nerve fascicle is preserved. (Bodian fuchsin stain $\times 70$).

the perimysium of the surrounding muscles. These fibers were lost for ultimate function.

The formation of thick and well developed axis cylinders was rarely observed in the distal segment 30 days after the suture in contrast to the large amount of fine nerve fibers present but was well under way after 45 and 60 days. The formation of myelin sheaths was practically absent after 30 days just beginning after 45 days and well recognized 60 days after suture. The amount of myelin decomposition products was large after 30 and 45 days and had only slightly decreased after 60 days (Fig. 4).

Even in the cat it was an exception that an autogenous graft healed like a nerve sectioned at two sites and repaired by end-to-end sutures. The ectodermal elements of the graft underwent a necrobiotic process and only the mesodermal elements remained alive. The myelin degeneration process was different from Wallerian degeneration. It also seemed that the Schwann cells became necrotic possibly as a result of ischemia. The mesodermal endoneurial cells however usually survived and were an important factor in the preservation of the original structure of the graft. They proliferated almost immediately after implantation of the graft and thus paved the way for the regenerating nerve fibers which

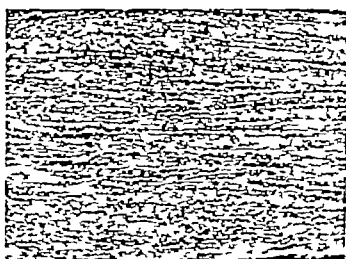


Fig. 7 Homogenous graft 60 days after transplantation showing a mixed isomorphous and heteromorphous structure and neurotization. There is a marked proliferation of mesodermal and Schwann cells and thick collagenous fibers run parallel to the regenerating nerve fibers (Bodian fuchsin stain $\times 95$).

accompanied by outgrowing Schwann cells followed the old endoneurial tubes (Fig. 5). Even in the most favorable such an isomorphous¹ structure was never seen throughout the graft; there was always some irregularity or excess proliferation of the old endoneurium which caused some branching off and confusion of the regenerating nerve fibers especially in the periphery of the graft. The borderline between perineurium and nerve fascicles remained intact. Some regenerating nerve fibers from the suture lines which penetrated the proliferative epineurium of the graft and proximal and distal segments could be traced for short distances but usually got lost. Once the regenerating nerve fibers had reached the distal suture line they found their way satisfactorily through the mesodermal granulation tissue and the mesodermal fibers of the suture line into the distal nerve segment. Six days after implantation of an autogenous graft a purely mesodermal junction was established by the endoneurial mesodermal elements and the perineurium of the graft and proximal and distal segments. Regenerating nerve fibers



Fig. 6 Homogenous graft 60 days after transplantation showing an entirely heteromorphous structure and neurotization. The borderline between the perineurium and nerve fascicle has been destroyed and bundles of band fibers and regenerating nerve fibers pass between dense strands of proliferating collagenous fibers into the perineurium. (Bodian fuchsin stain, $\times 95$.)

¹The term "isomorphous" is used to describe the structure of a graft in which the original neurilemma tubes are preserved and form a straight downward and parallel pathway for the regenerating band and nerve fibers. It has a similar aspect to that of regenerating peripheral nerve which has undergone Wallerian degeneration. It is the term "heteromorphous" structure to characterize the disappearance of the original nerve structure with graft and its replacement by a network of mesodermal fibers which lead the regenerating band and nerve fibers in an irregular and deviating course.

the muscle or skin. Thus in an average cat, the proximal site of repair lies 50 millimeters above the division of the sciatic nerve. The sural nerve leaves the sciatic nerve 40 millimeters below the site of suture. The length of nerve between the proximal site of repair and the entrance into the lateral head of the gastrocnemius is 80 millimeters; the medial head of the gastrocnemius 75 millimeters; the anterior tibial, 120 millimeters; the extensor digitorum longus 130 millimeters; and the flexor digitorum longus, 105 millimeters. The distance to the ankle along the tibial nerve measures 185 millimeters and along the deep peroneal nerve 190 millimeters. The length of the deep peroneal nerve and its divisions from the transverse ligament of the ankle to the proximal border of the foot pad is 60 millimeters and of the tibial nerve and its divisions to the base of the metatarsal bones, 60 millimeters.

MOTOR SIGNS OF RECOVERY

a Gait and stance The majority of the experimental animals were cats which normally walk and stand on the plantar surface of their toes only. It is only in the sitting position that the entire foot touches the ground. Paralysis of the muscles below the knee produced a gait characterized by a dragging forward of that extremity so that the toes were passively plantar flexed by friction on the floor. The animal thus bore its weight on the dorsum of the toes instead of the plantar surface. This is described hereafter as toe drop. In walking it appeared that the cat was able to elevate the heel from the floor even though the gastrocnemius muscle group was completely paralyzed. This lifting of the foot is performed by muscles above the knee which raise the knee and the leg. When the animal stood still and bore its weight on the posterior foot pads it was then apparent that it could not elevate the paralyzed heel from the floor. This is described hereafter as heel drop.

The disappearance of the heel drop sign was not a sign of early recovery of gastrocnemius function as one could demonstrate movements in the gastrocnemius muscle group by other means sometime before the

cat had enough power to elevate the heel off the floor when standing. For a similar reason, the disappearance of the toe drop could not be considered as a sign of early recovery of the anterior tibial muscle group. Furthermore, in some instances the cats developed contractures of the plantar flexors of the toes and of the dorsal flexors of the foot so that they never regained the ability to walk and stand on the toe pads even though they had good function in the dorsal and plantar flexors of the foot and toes.

In the animals which recovered without complications, normal gait and normal stance were regained. Following end to-end sutures heel drop started to disappear 45 days after nerve repair and a nearly normal standing position was regained after 60 days. Toe drop remained present after 60 days and began to disappear 90 days after nerve repair. In autogenous grafts heel drop started to recover after 60 days. It had disappeared in 66 per cent of the animals after 90 days and was practically gone 150 days after implantation of the graft. Toe drop was present in all cases after 75 days and began to disappear in 17 per cent of the animals after 90 days. However it was still present in 50 per cent of the animals 150 days after implantation of the graft. In homogenous grafts heel drop was present in all animals after 75 days; it began to disappear after 120 days and after 150 days all animals showed some recovery. Toe drop was present in all animals 150 days after implantation of the graft.

b Motion Motion was tested by provoking contractions of the leg and foot muscles by painful stimuli, such as tapping the site of nerve repair compressing the area of emergence of the roots of the sciatic nerve from the spinal column pressing upon the bones of the leg foot and toes and by pinching the skin of the leg and foot. To ascertain thus the presence of motion it was necessary to fix the knee or the ankle joint at a right angle in order to avoid the occurrence of supplementary motion resulting from movements of the thigh or hip. By these methods, recovery of motor function was detected earlier than was the appearance of normal gait or stance, or the recovery from heel drop. The earliest

movement elicited was plantar flexion of the foot followed by plantar flexion of the toes and dorsiflexion of the foot. Dorsiflexion of the toes and fanning of the toes appeared much later.

Plantar flexion of the foot could be produced in all end-to-end suture experiments after 60 days. In autogenous grafts this movement appeared between the 60th and the 82nd day averaging 70 days after implantation of the graft. In the same graft the average day of appearance of plantar flexion of the toes was the 71st and of dorsiflexion of the foot the 79th day. Dorsiflexion of the toes could be provoked only in 33 per cent of the animals at the 90th day and in 60 per cent on the 120th day and fanning of the 5th toe alone in 17 per cent of the animals on the 76th day and 80 per cent on the 120th day. In homogenous grafts occasionally some isolated motion could be produced 60 days after implantation but even after 90 and 120 days very few voluntary movements could be elicited.

MUSCULAR CONTRACTURES

In order to study the presence and degree of muscle contracture the normal and the operated upon extremities were examined at the same time and in the same fixed position. Muscular contractures manifested themselves by a limitation in the range of motion in the involved joint. Usually the contractures were mild so that with a little tension the muscle groups could be stretched to their normal length. In other instances the contractures were so obvious and so rigid that tension produced pain and did not increase the range of motion.

No significant contractures were found in the hamstring muscles and the knee could be extended in all cases. Neither were significant contractures found in the gastrocnemius muscle group; the feet could always be easily flexed against the anterior surface of the leg.

In testing the contractures of the anterior tibial muscle the knee was passively extended and the ankle would assume a position of 180 degrees extension. A slight contracture of the anterior tibial muscle was occasionally present usually less than 30 degrees so that

the ankle could be extended to about 150 degrees. The extensor digitorum longus was examined with the knee flexed at a right angle and when normal the ankle could be extended to 180 degrees. Contracture of this muscle group was the most common. It was usually associated with contracture of the dorsiflexors of the foot but was much more involved. In some cases it was present alone. The contractures of this muscle varied between 15 and 90 degrees. In the case of 90 degree contractures the ankle could not be extended further than a right angle with the leg.

The flexor digitorum longus was examined when the ankle was maintained at a right angle and the knee in an acute degree of flexion. The toes could then normally be dorsiflexed 90 degrees and plantar flexed 90 degrees from the horizontal. When the flexors of the toes were contracted the dorsiflexion was limited and in extreme cases the toes could not be moved from extreme plantar flexion which would represent a 180 degree contracture. Contractures of the flexor digitorum longus were less common than those involving the dorsiflexors of the toes and foot but when this muscle group was involved the contractures were usually more severe and 90 and 180 degree contractures were not uncommon.

Only the obvious contractures have been taken into consideration in the majority of the animals. None was observed in 30 animals with end-to-end sutures kept alive for various periods of time up to 90 days. Among a group of 39 animals with autogenous grafts two severe contractures of the extensor digitorum longus and one of the flexor digitorum longus were observed. In another group of 20 animals with autogenous grafts especially studied from a clinical standpoint the anterior tibial muscle group showed mild contractures in 6 animals rating from 15 to 30 degrees; the extensor digitorum longus showed contractures in 8 cases, 6 of them associated with the previous group and the extent of the contractures varied from 15 to 70 degrees. The flexor digitorum longus showed contractures in 5 cases, 2 of 15 degrees, 1 of 30 degrees and 2 of 90 degrees. Thus contrac-

tures were noticed to some degree in 55 per cent of this group of autogenous grafts. They were first noticed after 21 days in 1 animal, 30 days in 3 animals, 45 days in 2 animals, 60 days in 2 animals, and 70 days after implantation of the graft in 2 animals. These cats were allowed to live 90 or 120 days and the extent of the contractures increased in severity. In a group of 50 homogenous graft animals severe contractures were noticed in 6 cases and involved especially the extensor digitorum longus muscle group.

Obviously most of the contractures occurred during the stage of complete denervation and were a result of the bad position assumed by the paralyzed extremity described here as toe and heel drop. The former produced a shortening of the plantar flexors of the toes and the latter a shortening of the dorsiflexors of the foot and toes. Motor recovery and response to direct electrical stimuli were observed in the contracted muscles as well as in the other normal ones.

MUSCLE ATROPHY

Atrophy took place in all of the muscles temporarily denervated. The loss of muscle weight was directly proportional to the period of denervation. It reached its peak between the 15th and 45th day and as reinnervation took place the paralyzed muscles slowly and gradually regained weight.

During the examination it was always obvious that the gastrocnemius muscle group had lost a large amount of its volume and often could be palpated as a small stringlike organ. This was especially true and noticeable in animals with homogenous grafts. At autopsy the gastrocnemius and plantaris muscles were removed in one group and weighed, the affected side being compared to the healthy side. In a certain number of animals the anterior tibial and the extensor digitorum longus muscles were weighed and compared. The range of atrophy varied and remained wide even within the groups of animals which were allowed to recover the same length of time. The loss in weight in the gastrocnemius muscle group was usually larger than in the anterior tibial group. The amount of muscle atrophy was obviously higher in all of the

animals in which the distal suture line of the graft had been resected and resutured because this procedure prolonged the time of denervation. For this reason this group cannot be compared to animals in which the distal suture line was not resected.

Thirty days after end-to-end sutures, the loss of weight of the gastrocnemius muscle varied between 53 and 64 per cent. In 90 day old autogenous graft experiments the loss of weight of the gastrocnemius was between 18 and 39 per cent, the average being 30.4 per cent and in the anterior tibial muscle it varied between 19 and 46 per cent with an average loss of 26.4 per cent.

Comparing animals with autogenous and homogenous grafts which had undergone the same kind of treatment for the same period of time the gastrocnemius lost an average of 59 per cent of its weight within 90 days in autogenous and 72 per cent in homogenous grafts. One hundred and fifty days after implantation of the grafts the average loss of weight for the same muscle group was 45 per cent in autogenous and 54 per cent in homogenous grafts.

It is of interest to note that the specific gravity of the atrophied muscles was constantly slightly less than that of normal muscles. Comparing the diseased to the healthy muscles in autogenous grafts, the average specific gravity of the gastrocnemius muscle group was 1.0605 to 1.0675 and of the anterior tibial group 1.0611 to 1.0698.

Another interesting fact is that in animals which were allowed to recover 21 to 33 months after nerve repair the formerly paralyzed and atrophied muscle groups showed a tendency to become hypertrophic. Thus in a group of 5 animals with autogenous grafts, 5 animals with homogenous grafts and 1 end-to-end suture animal hypertrophied muscles were found in 8 instances. When compared to the same muscle groups of the healthy side they showed an increase in weight up to 15 per cent. In some cases only the anterior tibial group or the gastrocnemius group showed some hypertrophy while the opposite group was still slightly atrophied. In 5 of the 11 animals hypertrophy was present in both muscle groups. Three animals still showed

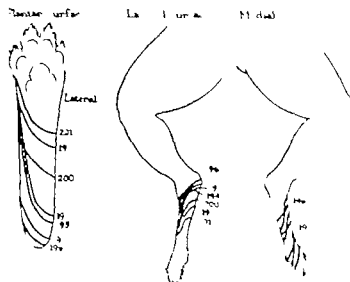


Fig 8 Composite chart of the area of analgesia in a group of cats 90 days after transplantation of an autogenous graft in the left sciatic nerve. The numbers indicate the identification number of the animal.

marked atrophy from 18.3 to 49.5 per cent in the gastrocnemius group and from 4.2 to 6.7 per cent in the anterior tibial group 23 to 25 months after nerve repair. The cases in which this severe atrophy was present were also characterized by marked muscle contractures and two of the three animals had large heel ulcers which did not show any tendency to heal. The animals with the hypertrophic muscles had no or minimal contractures and no trophic ulcers.

SIGNS OF SENSORY RECOVERY

The only sensation that could be tested was that of pain as evidenced by response to pin prick and pressure or deep pain.

a. Response to pin prick. The pin pricks were started in the anticipated anesthetic area and carried upward on the extremity until the cat gave some recognition of pain by crying or withdrawing the extremity. In this manner the anesthetic area could be demarcated. Pain sensation was tested 30, 45, 60 and 75 days after nerve repair. Marked differences in the area of analgesia were present in the animals tested during the same post operative periods. Since the site of nerve repair was approximately the same in all animals these differences were probably due to anatomical variations in the sensory supply and the degree of overlap to those areas. Thus in some animals, 30 days after end-to-end

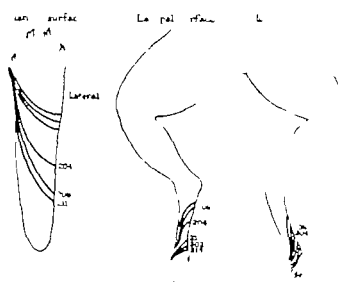


Fig 9 Composite chart of the area of analgesia in a group of cats 120 days after transplantation of an autogenous graft in the left sciatic nerve. The numbers indicate the identification number of the animal.

suture the analgesic area on the medial surface of the foot extended from the heel downward while in the other animals it was localized to the phalanges of the 2nd toe. In all animals however the entire lateral and plantar surfaces of the foot were completely analgesic. For this reason the return of sensation on the medial and dorsal surfaces of the foot could not be considered as a criterion for recovery.

The area of isolated sensory supply to pain of the sciatic nerve in the cat consists of the lateral and plantar surfaces of the foot and also includes the lower third of the lateral surface of the leg. In the other areas an overlap of sensory function by adjacent uninjured nerves such as the long saphenous must be considered. The critical areas of sensory recovery were thus limited to the external and the plantar surfaces of the foot and to the toes.

In end-to-end sutures no response to pin prick could be obtained below the heel after 30 and 45 days. Sixty days after suture pain sensation could be found around the heel in the area covering approximately one fourth of the plantar and lateral surfaces of the foot.

In autogenous and homogenous grafts no critical return of pain sensation was found after 75 days. Sixty days after secondary resection and resuture of the distal suture line of the grafts sensory recovery was occasionally

found in the case of autogenous grafts in a small area extending up to 2 centimeters distal from the heel. No critical sensory return was found in homogenous grafts even 75 days after resuture of the distal suture line. In a group of animals 90 days after the implantation of an autogenous graft return of pain sensation was observed in all of the animals in the area extending from the heel to half of the lateral and plantar surfaces of the foot (Fig 8). In a group of animals 120 days after the implantation of an autogenous graft the area of sensory return extended from the middle of the plantar surface to the proximal border of the foot pad and on the lateral surface from its middle to the beginning of the proximal phalanx of the fifth toes (Fig 9).

In long term animals complete sensory recovery was found 1 year after the implantation of autogenous or homogenous grafts as well as after repair by end to-end suture.

b Response to pressure or deep pain. Compression of the toe pads produced a response observed as a withdrawal of the whole extremity. This withdrawal sign was considered as a test performed by muscles above the knee. After section and repair of the sciatic nerve the animals did not respond to compression of the toe pads for a long period of time. It was considered that the extent of isolated loss of deep sensation of the sciatic nerve that could be tested with any degree of accuracy was restricted to the pads of the 2nd, 3rd, 4th, and 5th toes.

The earliest response to deep pain was observed on compression of the 2nd toe. It was occasionally elicited 30 days after an end to-end suture but was present in only 50 per cent of the animals 60 days after end to-end suture. At that time 30 per cent of the animals responded to compression of the other toes as well.

After repair by autogenous and homogenous grafts response to compression of the 2nd toe was rarely present within the first 75 days. This isolated response however was present in most autogenous grafts 60 and 75 days after secondary resection and resuture of the distal suture line of the graft and a response from compression of the 3rd and 4th toes

was also obtained in rare instances. In homogenous grafts even 75 days after resection and resuture of the distal suture line withdrawal following compression of the 2nd toe was rare.

In a group of animals 90 days after repair by an autogenous graft no response to deep pressure was obtained in 28.5 per cent of the cases, while 71.5 per cent responded to compression of the 2nd toe and 43 per cent to compression of all toes. In a group of animals 120 days after an autogenous graft repair 16 per cent did not respond to deep pressure while 84 per cent responded to compression of the 2nd toe and 66 per cent to compression of all toes.

SIGNS OF TROPHIC DISTURBANCES

The foot and the four toe pads of the cat are normally soft moist and very sensitive to pain. After section of the sciatic nerve they became pale dry thick coarse and horny and desquamation of the horny layer took place. These skin changes persisted a long time after repair of the sectioned nerve. They remained that way 60 days after end to-end suture and 75 days after the implantation of grafts.

In a group of 90 autogenous graft experiments, a slight change was found in the foot pads of only 14 per cent of the animals. When recovering they first lost their thick and horny appearance and became soft, still they remained dry. One hundred and twenty days after implantation of an autogenous graft 50 per cent of the animals showed some recovery in the texture and the appearance of the foot and toe pads.

Another trophic change which occurred was the formation of an ulcer on the plantar surface of the heel. Normally a cat never stands or walks on its heel and the skin of the heel is delicate. The lesion of the heel was in most cases very mild and consisted in a circular loss of hair and thickening of the underlying skin. In a small group of animals, however, an ulcer developed and produced marked inflammatory reactions. The ulcers showed a soft necrotic and bleeding base which was surrounded by a thick circular wall. The animals developed the ulcers between the 30th

and 45th day after nerve repair. Most of them occurred after implantation of grafts especially if the graft was homogenous.

Only one of the 30 animals developed an ulcer (3.3 per cent) after end-to-end suture. 4 of the 65 animals with autogenous grafts developed an ulcer (6.2) and 6 of the 50 animals with homogenous grafts had an ulcer (12 per cent). In some cases the ulcers healed spontaneously 45 to 60 days after their appearance. Most of them however persisted until the specimen was removed in 2 cases the ulcer was still present after the 25th month. Eight animals which had no heel ulcer developed one after secondary resection and resuture of the distal suture line of the graft. 3 of these had autogenous and 5 homogenous grafts. In 2 animals the ulcer involved the bone and marked contractures developed fixing the foot at a right angle with the leg and preventing dorsiflexion of the toes.

Some limitation of movements was present in some of the other cats which had ulcers but it was not more prominent than in the animals which had no ulcers. The ulcers retarded clinical recovery as they were painful and the animal avoided movement of the leg and avoided stepping on the affected foot. Large suture line neuromas were found in 3 cases which had developed ulcers and in 5 cases the amount of adhesions around the grafts and the suture lines was large but the microscopic sections showed good neurotization of the distal nerve segment. Response to electrical stimulation however showed the normal signs of recovery in all of the tested muscle groups.

The claws on the affected side were usually longer and thicker on the normal side. Sheathing of the claws was occasionally observed together with the recovery of the texture and appearance of the foot and toe pads but these observations were not followed sufficiently well to ascertain the return to normal appearance and growth of the claws.

RETURN OF REFLEXES

The *fanning reflex* is elicited by allowing the cat to fall rapidly when it is suspended by the skin of the back of the neck. The toes of the

normal side fan out but on the paralyzed side the toes remain together and no fanning occurs.

This reflex is a very late and inconstant sign of recovery and when it is present it is usually incomplete. In a few isolated cases an abduction of the 5th toe alone has been observed while the other 3 toes did not move when the animal was dropped. The abduction of the 5th toe however is produced by a contraction of an isolated muscle of the leg the peroneus tertius which is supplied by a branch of the superficial peroneal nerve. The fanning of the other toes is produced by contractions of the short muscles of the foot and toes supplied by distal branches of the deep peroneal nerve.

The fanning reflex of the 5th toe was observed in one case of end-to-end suture after 60 days in 2 cases of autogenous grafts after 60 days in one autogenous graft after 80 days and in another one after 90 days. In a group of 13 end-to-end sutures autogenous and homogenous graft experiments which were allowed to recover for a period of 2 to 3 years a slight fanning reflex of all the toes was observed only once and that occurred in an animal with a homogenous graft.

Fanning of the toes as a response to direct electrical stimulation of the nerve is also a late sign of recovery but it has been obtained in a large number of animals in which the reflex could not be elicited. The same applies to the fanning of the toes obtained as a response to painful stimuli.

The *step reflex* is elicited by suspending the cat by the back of the neck and permitting the dorsal surface of the hind paws to rub lightly against the projecting edge of a table. On the normal side the whole lower extremity responds by a step-like movement while the paralyzed extremity hangs limply without response. When function returns a slight dorsiflexion of the foot occurs which is later followed by a slight plantar flexion of the foot, producing feeble step-like movements. This beginning return of the step reflex has been found only in isolated animals a long period of time after nerve repair. A normal step reflex which also included movements of the toes has never been observed even in animals which were allowed to recover for 34 months.

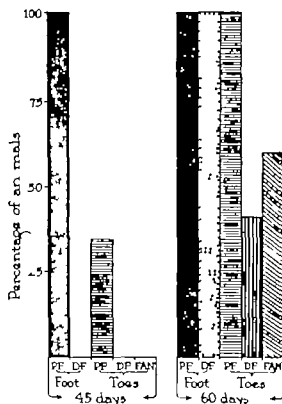


Fig. 9. Response of various muscle groups to direct electrical stimulation of the sciatic nerve 45 and 60 days after end to end suture. PE plantar flexors, DF dorsiflexors, FAN abductors and adductors.

The *Achilles reflex* was not constantly tested as it is difficult to obtain in a normal cat. It was observed in a few animals 90 and 120 days after the implantation of an autogenous graft and it occasionally seemed to be more active than on the healthy side.

All reflexes were found to be late and in constant signs of recovery. They could be elicited only in a very small number of animals and thus are of no great statistical value.

RESPONSE TO ELECTRICAL STIMULATION

Whenever it was necessary to expose the repaired sciatic nerve whether it was when the specimen was removed or when the distal suture line of the graft was resected and resutured the nerve was electrically stimulated and the responses were tabulated. Stimulation was performed with a stimulator designed by Hinsey and Geoghean which produced an alternating current of sine wave form of a frequency of 60 cycles per second and made it

possible to measure the voltage necessary to produce a muscular contraction. The exposed nerve was stimulated with platinum electrodes at various levels above on or below the suture lines and on the grafts. The tibial and the common peroneal nerves were stimulated in the popliteal fossa and the tibial and the deep peroneal nerves at the level of the ankle. The reading of the voltmeter was taken when the stimulus was strong enough to produce a definite motion as a result of small contractions of the flexor or extensor groups of the foot or toes. Thus the following motions were considered: plantar flexion of the foot, plantar flexion of the toes, dorsiflexion of the foot, dorsiflexion of the toes, fanning of the 5th toe, fanning of all toes, inversion and eversion of the foot, abduction of the heel, flexion and extension of the proximal phalanges of the toes. For critical examination the least amount of current necessary to produce plantar flexion of the foot and toes, dorsiflexion of the foot and toes and fanning of the toes was recorded. In the normal sciatic nerve the average threshold needed to produce these various movements was 0.1 volt.

a End-to-end sutures. No response was obtained from 30 day animals. In the 45 day group 33 per cent of the animals had 40 per cent of the normal total electrical response, and 67 per cent gave 20 per cent of the normal response. This means that 100 per cent of the animals responded with plantar flexion of the foot and 33 per cent with plantar flexion of the toes. In the 60 day group 30 per cent of the animals scored 100 per cent electrical response, 40 per cent scored 80 per cent and 30 per cent scored 60 per cent of the total electrical responses. Considering the various muscle groups, 100 per cent of the animals had plantar flexion of the foot, plantar flexion of the toes and dorsiflexion of the foot while only 40 per cent responded with dorsiflexion of the toes and 60 per cent with some fanning of one or more toes (Fig. 10).

b Autogenous grafts. No response was obtained from electrical stimulation of the nerve or graft 45 days after implantation of the graft. In 60 day old grafts plantar flexion of the foot and plantar flexion of the toes could be obtained in 33 per cent of the animals.

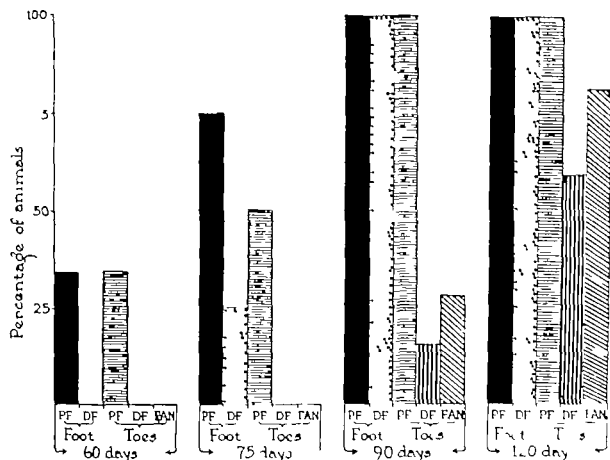


Fig. 11. Response of various muscle groups to direct electrical stimulation of the sciatic nerve 60, 75, 90, and 120 days after transplantation of an autogenous graft. PF, plantar flexors; DF, dorsiflexors; FAN, abductors and adductors.

In 75 day old grafts plantar flexion of the foot was obtained in 75 per cent plantar flexion of the toes in 50 per cent and dorsiflexion of the foot in 25 per cent of the animals. In 90 day old grafts plantar flexion of the foot and toes and dorsiflexion of the foot was obtained in 100 per cent dorsiflexion of the toes in 14 per cent and fanning of the toes in 29 per cent of the animals. In 120 day old grafts plantar flexion of the foot and toes and dorsiflexion of the foot was present in 100 per cent dorsiflexion of the toes in 60 per cent, and fanning of the toes in 80 per cent of the animals (Fig. 11).

After resection and resuture of the distal suture line of the grafts the responses were slightly changed. Forty five days after resection 78 per cent of the animals presented plantar flexion of the foot and dorsiflexion of the foot 47 per cent plantar flexion of the toes, and 6 per cent fanning of the toes. Sixty days after resection 100 per cent showed plantar flexion of the foot 90 per cent plantar flexion of the toes 72 per cent dorsiflexion of

the foot and 9 per cent fanning of the toes. Seventy five days after resection plantar flexion of the foot was obtained in 90 per cent dorsiflexion of the foot in 78 per cent plantar flexion of the toes in 66 per cent and fanning of the toes in 22 per cent of the animals. Ninety days after resection plantar flexion of the foot and toes and dorsiflexion of the foot were obtained in 100 per cent fanning of the toes in 43 per cent and dorsiflexion of the toes in 14 per cent of the animals. It is interesting to note that dorsiflexion of the toes was obtained only in the 90 day group of animals after secondary resection and resuture of the distal suture line of the graft.

c. Homogenous grafts. No response to electrical stimulation could be obtained 45 and 60 days after implantation of the graft and after 75 days 25 per cent of the animals responded with plantar flexion of the foot.

Forty five days after resection and resuture of the distal suture line of the graft 6 per cent of the animals showed plantar flexion of the

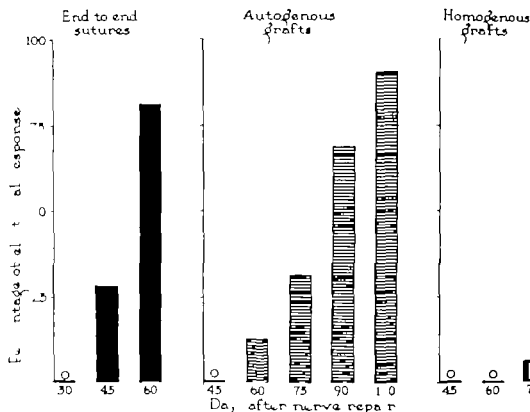


Fig. 2. Average score of total muscular response to direct electrical stimulation of the sciatic nerve repaired by end-to-end suture or by transplantation of an autogenous or homologous graft after various periods of time.

foot, 37 per cent plantar flexion of the toes, 28 per cent dorsiflexion of the foot and 9 per cent dorsiflexion of the toes. Sixty days after resection plantar flexion of the foot was obtained in 100 per cent, plantar flexion of the toes in 85 per cent, dorsiflexion of the foot in 56 per cent, dorsiflexion of the toes in 35 per cent and fanning of the toes in 21 per cent of the animals. For some unknown reason the group of animals tested 75 days after resection does not fit in the pattern of the usual responses to electrical stimulation. Plantar flexion of the foot was shown by 76 per cent, plantar flexion of the toes by 50 per cent, dorsiflexion of the foot by 40 per cent, dorsiflexion of the toes by 60 per cent and fanning of the toes by 31 per cent of the animals.

The nerves repaired by end-to-end suture showed earlier and better responses to electrical stimulation than did those in which grafts were used. Electrical stimulation was also seen earlier in autogenous than homologous grafts (Fig. 12). After resection and

resuture of the distal suture line of the graft, the difference between response in both kinds of grafts was much less evident although it remained slightly better in the autogenous grafts (Fig. 13).

Plantar flexion of the foot was the first response to be observed and it was closely followed by plantar flexion of the toes and dorsiflexion of the foot. Dorsiflexion of the toes and fanning of the toes were late responses. The amount of current needed to produce the responses varied between 0.01 and 0.9 volts. The more the nerve regeneration had progressed the less current was necessary to get a response. A constant observation was that less current was needed when the suture lines were stimulated and slightly more when the proximal and distal nerve segments were stimulated. Response to stimulation of the nerves at the ankle was obtained 60 days after end-to-end suture and 90 days after resected autogenous grafts. In animals with 120 day autogenous grafts stimulation of the tibial

nerve at the ankle produced a plantar flexion of the proximal phalanges of the toes in 100 per cent of the animals and stimulation of the deep peroneal nerve a dorsiflexion of the proximal phalanges in 80 per cent and a fanning of all toes in 40 per cent of the animals.

B GUNSHOT EXPERIMENTS

The aim of the study upon experimental gunshot injuries was to produce a wound with tissue destruction and severance of the sciatic nerve the severity of which could be compared to the usual wounds of modern warfare.

The experimental methods and technique have been described in another paper. In brief however repair of the nerve was effected by an end-to-end suture or by the implantation of a homogenous graft.

MICROSCOPIC STUDY

When a cat's nerve is struck by a bullet severely enough only to cause a contusion and not an interruption of nerve continuity the myelin sheaths break down in a similar manner but to a greater degree than is seen following sharp severance of a nerve. There is a molecular decomposition of the myelin with a localized edema—a process best called necrobiotic (Fig. 14) and entirely different from a secondary or Wallerian degeneration (Fig. 15). This necrobiosis occurs under conditions which have one factor in common—the damage to the myelin sheaths in combination with an apparent damage to the Schwann cells with survival of the mesodermal endoneural elements. The damage to the Schwann cells seems to concern chiefly their proliferating decomposition activities. They are not destroyed in milder traumatic damage where the axis cylinders are seen to survive the demyelination. They enter into action in later nerve fiber regeneration and remyelination but fail in digesting the myelin.

Stimulation of the mesodermal cells preceding nerve fiber regeneration by the nonfatty myelin decomposition products is very clearly seen and leads wherever the traumatic lesion has reached a certain severity to a confusion of the original endoneural structure and by necessity to a bewildering and irregular overproduction of regenerating nerve fibers.

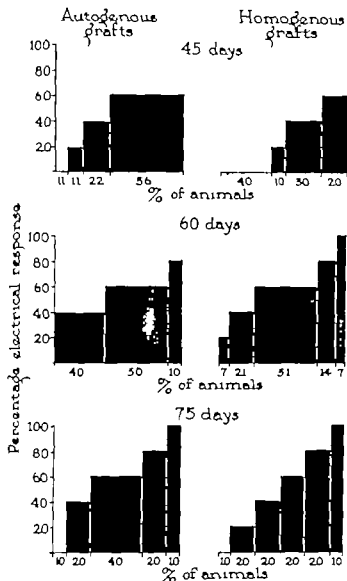


Fig. 13. Comparison between the percentage of animals and the percentage of muscular response to direct electrical stimulation of the sciatic nerve repaired by transplantation of autogenous or homogenous grafts 45, 70, and 75 days after secondary resection and resuture of the distal suture line of the grafts.

A heteromorphous nerve structure results. At a period when the neurotization is already well advanced the myelin-detritus can still be seen between the endoneural tubes and fibers (Fig. 16). Mesodermal macrophages play the great part in its elimination.

Degrees of structural damage in such contused nerves may be found. The nerve with the slightest damage may show very little axis cylinder degeneration and for this reason only a relatively short transient disturbance of function whereas in severe contusion even without any visible macroscopic nerve lesion a complete Wallerian degeneration of some or



Fig. 4.



Fig. 5.

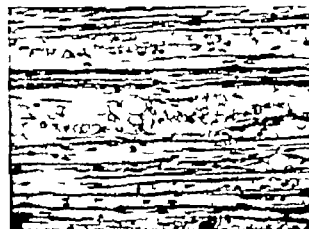


Fig. 6.



Fig. 7.

Fig. 4. Contusion of the sciatic nerve 6 days after a gunshot injury. This shows the predominantly destructive reaction of the axis cylinders within the proximal nerve segment. Some of the axis cylinders are swollen and show signs of disintegration. A relatively well preserved axis cylinder is surrounded by swollen and partly vacuolated sheath. In other portions the myelin sheaths are partly or completely destroyed. Large amounts of detritus and edema are present mostly between the endoneurial sheaths, and histiocytic elements are scattered within them. There is general cellular proliferation of the endoneurial cells, beginning proliferation of Schwann cells, and regenerating nerve fiber is clearly visible in the center of the picture (Bodian-fuchsin stain, $\times 450$).

Fig. 5. Contusion of the sciatic nerve 6 days after gunshot injury. It shows the distal nerve segment of the same specimen as in Figure 4, with the typical aspect of secondary degeneration. Remnants of broken down axis cylinders, degenerated myelin sheaths with myelin globules, vacuoles, and beginning cellular reaction are present. (Bodian-fuchsin stain, $\times 450$).

Fig. 6. Contusion of the sciatic nerve 45 days after a gunshot injury. The distal nerve segment shows secondary degeneration and some traumatic myelin destruction. Neutral fats lying mostly within the detritus cells are accumulated near capillaries. Endoneurial proliferation and nerve fiber regeneration are pronounced. (Weil stain, $\times 450$).

Fig. 7. Contusion of the sciatic nerve 60 days after a gunshot injury showing a severely traumatized nerve in full regeneration with heteromorphous structure and type of neurotization. Large amount of detritus are still present. The upper half of the photomicrograph shows the neurotization aspect of the epineurium. In this case the bullet had traumatized the epineurium and had produced a gap in the perineurium through which numerous regenerating nerve fibers entered the epineurium. The proliferation of mesodermal cells in the epineurium was accompanied by diffuse nerve fiber regeneration. Such also followed the granulation tissue of the epineurium into the adjacent muscle. The course of these regenerating nerve fibers is very irregular and just as many are seen in cross as in longitudinal sections. (Bodian-fuchsin stain $\times 75$).

all nerve branches in combination with the heteromorphous type of endoneurial proliferation and neurotization will be accompanied by a clinical picture similar to that produced

by section of a nerve. These observations explain why some nerve contusions are followed by hardly any or only limited interruption of motor and sensory function where-



Fig 18. Proximal segment of the sciatic nerve 30 days after end-to-end suture in a gunshot injury showing the heteromorphous structure and neurotization in the traumatic zone. Myelin decomposition products are still present. Diffuse proliferation of the ectodermal and mesodermal endoneurial elements creates a confusing course for the regenerating nerve fibers. A marked Perroncito spiral formation is present. (Bodian fuchsin stain, $\times 165$)



Fig 19. Homogenous graft 30 days after transplantation into the sciatic nerve following a gunshot injury. Structure and neurotization are typically heteromorphous. Dense strands of proliferating collagenous fibers are present within the entire course of the graft. No differences were encountered in the structure of the homogenous grafts following gunshot injuries of sharp sections. (Bodian-fuchsin stain $\times 190$)

as in other cases contusion leads to complete paralysis and often only imperfect return of function.

Nerve contusion may interrupt the continuity of the perineurium of nerve fascicles. This leads to a herniation of regenerating nerve fibers into the epineurium and formation of traumatic neuromas. Here again the primary endoneurial fibroblastic proliferation through the perineurial gap results in the sprouting of regenerating nerve fibers into the epineurium (Fig 17). These fibers are of course lost for the neurotization of the degenerating part of the nerve distal to the injury.

The cat's sciatic nerve severed by a bullet differs greatly in its histological aspects from a sharply sectioned nerve. The traumatic destruction described is much more severe and extends centralward in the proximal segment not just a few millimeters but very frequently several centimeters. This same effect may be seen reaching just as far distally in the distal segment of the damaged nerve. The effect on regeneration manifests itself in the heteromorphous type of organization and neurotization of the whole traumatized area (Fig 18). This change is accompanied at the suture line by a greater epineurial proliferation and with this there was noted an increase in the number of deviating nerve fibers fanning out from the

proximal segment. This strong mesodermal reaction again seemed to be in direct proportion to the number of deviating nerve fibers.

The effect of this confusion and blockage of nerve fibers near and at the suture line of the gunshot end-to-end repair experiments is somewhat difficult to estimate in a quantitative manner but a study of the distal nerve segments can be roughly tabulated for the sake of comparison. Microscopic examination of nerves sutured end-to-end after sharp section showed regenerated nerve fibers in the distal segment after 30 days (plus 2) in all cases while this was increased (plus 3) after 45 and 60 days. In the gunshot specimens the regenerated nerve fibers were just beginning to be present at the end of 30 days (plus 1) while they had further progressed at the end of 45 days (plus 2) and were quite satisfactory (plus 3) at the end of 60 days. In the sharp section series the formation of thick, well developed axis cylinders in contrast to numerous fine regenerated nerve fibers growing in the proliferative endoneurium of the distal segment was found to be insignificant after 30 days and well under way after 45 and 60 days. The formation of myelin sheaths was likewise practically absent after 30 days just beginning after 45 days and well established after 60 days. On the other hand it was found that in the gunshot specimens there was just a be-

gunning of myelin sheath formation and axis cylinder formation at 45 days. This had progressed only to the status of satisfactory at the end of 60 days in most instances and only rarely was considered well established by this time. Myelin decomposition products were found after 30 and 45 days (plus 3) in all cases of the sharp section series but were definitely less (plus 2) by the end of 60 days. The gunshot specimens showed a persistence of these decomposition products (plus 3) even up to 60 days. In all cases a moderate to severe amount of spongy fibrous proliferation of epineurium with marked hyperemia and some lymphocytic infiltrations was found over the central segment, and this was much more intense over the distal segment. There was also a moderately dense fibrous proliferation of the perineurium with increased vascularization and quite a few lymphocytic foci over both segments. It is true that a similar pattern was found in the sharp section series but this was quite minimal in comparison.

There were no notable differences between the homogenous grafts of the sharp section series and those of the gunshot series in so far as the histological picture is concerned except for an occasional instance of the reaction to trauma above mentioned (Fig. 19). The reason for this lies in the fact that a graft was used in the gunshot series after large amounts of traumatized nerve had been resected many times amounting to 3 or 3.5 centimeters. In such instances the graft then was sutured to fairly normal nerve which did not show the confusional pattern of the gunshot trauma.

MOTOR SIGNS OF RECOVERY

In the animals with end-to-end sutures no changes in the paralyzed extremity were noted at the end of 30 days that is they dragged the foot when walking the ankle was flail like and the toes were dropped so that the dorsum presented toward the floor. After 45 days, 8 out of 18 animals showed improvement by walking with less heel drop while after 60 days 10 out of 22 animals were improved. Of these latter 10 animals, 14 were able to stand with the heel off the ground. There was no evidence of return of function of dorsiflexion of the toes in any of the animals after 30 or 45

days but after 60 days 13 out of 22 animals no longer dragged their toes but walked with a plantar gait.

In the animals with homogenous graft there was no evidence of recovery 45 days after resection but in the 60 day resected group 11 out of 17 animals walked with the heel off the ground. In the 75 day resected group 14 out of 14 walked in this same fashion but only 1 stood with the heel well off the ground. In none of these animals was there recovery of movement of the toes. In comparison it is noted that 7 out of 12 180 day nonresected homogenous graft animals stood with the heel well off the ground and 5 of the 12 walked with a toe drop.

MUSCULAR CONTRACTURES

In most instances the contractures found were mild so that with a little tension the muscle could be stretched to its normal length. On the other hand a few contractures were quite obvious and no attempt to overcome them was successful especially in view of the pain produced by the maneuver of the examiner.

As far as individual muscles are concerned no significant contractures were found in the hamstrings or in the gastrocnemius muscle group that is the knee could be fully extended and flexed in practically all cases. The only exception to this was a rare instance in which a persistent draining sinus involved the hamstring muscle group. When changes were noted they were found in the anterior tibial muscles, in the common extensors of the toes, and in the plantar flexors of the toes. In the end-to-end sutures only 3 instances were found in 58 animals 2 occurring in 60 day animals and the third in a 75 day animal. Two contractures were classified as mild and a third as severe involving especially the flexor digitorum longus this latter case being complicated by a persistently draining sinus tract from the bullet wound.

In the grafts of 45 days duration no contractures were found in 8 animals, but after resection of the distal suture line 3 of these had mild contractures of the extensor digitorum longus at the end of the second 45 day period. In the 60 day group 2 mild contractures were

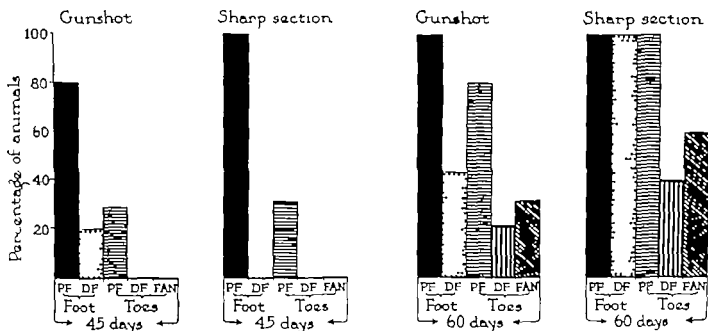


Fig. 30 Comparison of the response of the various muscle groups to direct electrical stimulation of the sciatic

nerve 45 and 60 days after end-to-end suture. PF, plantar flexors; DF, dorsiflexors; F4-V, abductors and adductors.

found before resection but 60 days after resection 7 of the 17 animals showed mild contractures of the dorsiflexors of the foot and in 3 animals severe contractures of the flexors of the foot and toes were present including two 90 degree and one 135 degree contracture of the flexor digitorum longus. In the 75 day animals with grafts mild contractures were found in 5 of 14 animals before resection while 75 days after resection 2 more showed mild contractures of the flexors of the foot and toes and 7 had a marked contracture of the anterior tibial muscle 3 of which immobilized the foot at right angles with the leg. These animals also had a severe contracture of the flexor digitorum longus and in 5 of them the toes could not be moved from a flexed position representing a 110 to 165 degree contracture. In the 12 animals with homogenous grafts allowed to go 180 days without resection of the distal suture line there were but 2 animals with contractures of moderate degree

MUSCLE ATROPHY

Sufficient data concerning muscle atrophy were obtained in only 25 animals of the gunshot series. In 3 animals with 60 day end-to-end sutures there was percentage weight losses of 51, 54, and 54, while 3 other animals with 75 day end-to-end sutures revealed percentage weight losses of 41, 49, and 50. These were

large losses but it must be remembered that these were very short experiments. This is more emphatically brought out when it is noted that a cat with a 15 month old end-to-end suture showed a weight loss of only 5 per cent. In the case of the homogenous grafts 3 cats revealed percentage weight losses of 50, 54, and 54 respectively 45 days after resection of the distal suture line while the average of nine 60 day and four 75 day animals similarly treated were 51 and 58 per cent, respectively. Again this should not be considered a maximum in recovery since a cat with a 16 month homogenous graft without resection of the distal suture line had a percentage weight loss of but 7.5 per cent. A further interesting comparison can be made with the finding of an average weight loss of 15.5 per cent in 12 animals with grafts of 180 days duration without resection of the distal suture line.

SIGNS OF SENSORY RECOVERY

In the animals with end-to-end sutures there were no instances of recovery to pin prick in areas of isolated supply up to 75 days.

In 4 of 9 animals 45 days after resection and resuture of the distal suture line of an homogenous graft performed 90 days previously there was some return of sensation to pin prick in the area of isolated supply. A similar return occurred in 10 of 17 animals with 60

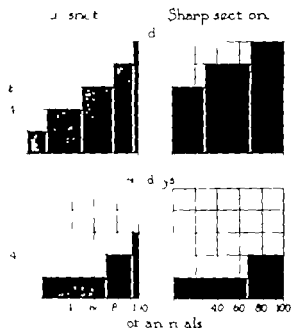


Fig. 1. Comparison of the percentage of muscular response to electrical stimulation of the sciatic nerve in end-to-end suture repair and sharp section of animals.

lay interval and in 9 of 14 animals with 75 lay interval.

There was a complete return of sensation to the foot at the end of 150 days in 10 end-to-end suture animals and at the end of 180 days in 1 cat with homogeneous grafts in which the distal suture line was not resected.

Deep pain or pressure pain produced by impression of the toe pad was present in 33 1/3 per cent of the animals 60 days after end-to-end suture in 11 per cent of the animals with homogeneous grafts in which the distal suture line was resected after 60 days and the examination 10 days after the graft had been surgically introduced. In 14 per cent of animals with homogeneous grafts with a resected distal suture line at the end of 75 days and 10 days after introduction of the graft there was a return of pressure pain. However, 10 per cent of 12 animals showed a response after 180 days without resection and return of the distal suture line.

RETURN OF REFLEXES

In 58 animals with short term end-to-end suture only two plantar ulcerations were found. Both of these occurred in 60 day ani-

mals, one of which had a severe contracture together with a chronically draining sinus tract originating from the wound site.

In the animals with 45 day homogeneous grafts, no ulcers were found in 10 animals before resection but one developed after resection. In the 60 day group 2 out of 17 animals developed ulcers before resection while 10 other 3 developed them afterward giving a total of 6 out of 14 at the end of 150 days. In the series of 12 animals with homogeneous grafts allowed to survive 180 days without resection of the distal suture line only 1 ulcer was found one involved the toes and the other the plantar surface of the heel.

RETURN OF REFLEXES

The step reflex was found in 40 per cent of the animals with end-to-end sutures of more than 25 days duration. In only 3 of 31 animals with homogeneous grafts of over 60 day duration was there evidence of a step reflex and this was a feeble response.

RESPONSE TO ELECTRICAL STIMULATION

Muscle responses to electrical stimulation were diminished in the case of end-to-end suture repair of severance by gunshot as compared with those of sharp division of the nerve.

The first observed response was plantar flexion of the foot. This was closely followed by the return of plantar flexion of the toes and dorsiflexion of the foot. Dorsiflexion of the toes and fanning of the toes were characteristically late findings although present in some animals at the end of 60 days.

After 45 days the gunshot injuries showed a response of plantar flexion of the foot in 76 per cent of the animals as compared to 100 per cent of the sharp section injuries. Plantar flexion of the toes 23 per cent and 33 per cent and dorsiflexion of the foot 17 per cent and 6 per cent respectively. In neither group was there a response of dorsiflexion of the toes or fanning of the toes. After 60 days there was a 100 per cent response of plantar flexion of the toes in both groups, 77 per cent of the gunshot animals showed the response of plantar flexion of the toes as compared to 100 per cent of the sharp division experiments. Dorsiflexion of the

TABLE I

Days	Percentage Recovery	
	Gunshot—%	Sharp section—%
45	30.2	31
60	52.2	57
75	58.5	53

foot 27 per cent and 100 per cent dorsiflexion of the toes 23 per cent and 40 per cent and fanning of the toes 32 per cent and 40 per cent respectively (Fig. 20).

Another interesting comparison was found by noting the highest percentage of animals possessing the greatest degree of motor response upon electrical stimulation in each time period. In the gunshot series 6 per cent of the animals had 60 per cent return of function at 45 days and 4.6 per cent had 100 per cent return of function at 60 days while the sharp section series showed 33 per cent of the animals with 40 per cent return of function at 45 days and 30 per cent with 100 per cent return of function at 60 days (Fig. 21).

In the homogenous grafts the average muscular response after resection of the distal suture line is shown in Table I.

Again the same progression of recovery of response in relation to time was found in both series but here it was noted that there was no great difference in the rate of recovery between the gunshot animals and the control series. This similarity is further brought out through the study of the breakdown of this recovery into terms of each function as shown in Table II.

TABLE II

	45 Days		60 Days		75 Days	
	Gunshot	Sharp section	Gunshot	Sharp section	Gunshot	Sharp section
PFF	88.8	50	100	100	100	76
PFT	25.5	37	40.0	85	64	50
DF	25.5	28	91	56	93	40
DFT	0	0	7	35	7.6	60
Fanning	13	0	20	2	25	30

PFF: plantar flexion of foot; PFT: plantar flexion of toes; DF: dorsiflexion of foot; DFT: dorsiflexion of toes.

With regard to the highest percentage of animals showing the greatest degree of muscle response in each time period in the 45 days resected distal suture line group 12 per cent showed 60 per cent return of function in the 60 day group 17.6 per cent showed 80 per cent return and 25 per cent of the 75 day group showed 80 per cent return of motion according to these criteria. This can be compared with

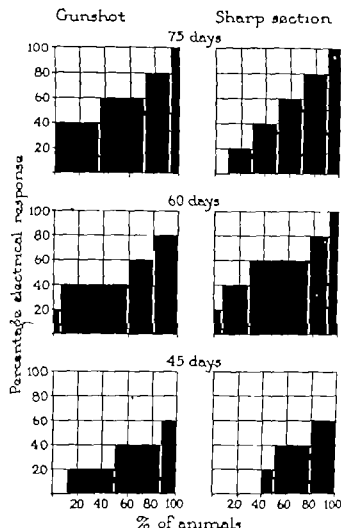


Fig. 22. Comparison of the percentage of muscular response to direct electrical stimulation of the sciatic nerve 45, 60, and 75 days after resection and resuture of the distal suture line of homogenous grafts in relation to the number of animals manifesting this recovery.

the sharp section series in which 20 per cent of the 45 day resected distal suture line graft animals showed 60 per cent of muscle response while 7 per cent of the 60 day animals and 10 per cent of the 75 day animals showed 100 per cent return of response (Fig. 22). On the other hand of 12 animals with nonresected distal suture line grafts of 180 days duration in the gunshot series 60 per cent revealed 100 per cent muscle response upon electrical stimulation.

SUMMARY

1. Swelling is always present at the suture lines in end-to-end sutures as well as in autogenous and homogenous grafts. The distal suture line of a graft is always larger than the proximal suture line and it is larger in a homogenous graft than in an autogenous graft. It

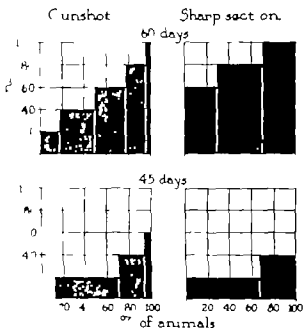


Fig. 1. Comparison of the percentage of muscular response to direct electrical stimulation of the sciatic nerve 45 and 60 days after end-to-end suture relation to the number of animals manifesting this recovery.

day intervals and in 9 of 14 animals with 75 day intervals.

There was a complete return of sensation to pin prick at the end of 10 days in 10 end-to-end suture animals and at the end of 180 days in 12 cats with homogenous grafts in which the distal suture line was not resected.

Deep pain or pressure pain produced by compression of the toe pads was present in 33.3 per cent of the animals 60 days after end-to-end suture, in 11.7 per cent of the animals with homogenous grafts in which the distal suture line was resected after 60 days and the examination made 120 days after the graft had been originally introduced. In 14.2 per cent of animals with homogenous grafts with a resected distal suture line at the end of 75 days and studied 150 days after introduction of the graft there was a return of pressure pain. However, 1 per cent of 12 animals showed a response after 180 days without resection and resuture of the distal suture line.

SIGNS OF TROPHIC DISTURBANCES

In 48 animals with short term end-to-end sutures only two plantar ulcerations were found. Both of these occurred in 60 day ani-

mals, one of which had a severe contracture together with a chronically draining sinus tract originating from the wound site.

In the animals with 45 day homogenous grafts no ulcers were found in 10 animals before resection but one developed after resection. In the 60 day group 2 out of 17 animals developed ulcers before resection while 2 other 3 developed them afterward giving a total of 6 out of 14 at the end of 150 days. In the series of 12 animals with homogenous grafts allowed to survive 180 days without resection of the distal suture line only 2 ulcers were found, one involved the toes and the other the plantar surface of the heel.

RETURN OF REFLEXES

The step reflex was found in 40 per cent of the animals with end-to-end sutures of more than 25 days duration. In only 3 of 33 animals with homogenous grafts of over 60 days duration was there evidence of a step reflex and this was a feeble response.

RESPONSE TO ELECTRICAL STIMULATION

Muscle responses to electrical stimulation were diminished in the case of end-to-end suture repair of severance by gunshot as compared with those of sharp division of the nerve.

The first observed response was plantar flexion of the foot. This was closely followed by the return of plantar flexion of the toes and dorsiflexion of the foot. Dorsiflexion of the toes and fanning of the toes were characteristically late findings although present in some animals at the end of 60 days.

After 45 days the gunshot injuries showed a response of plantar flexion of the foot in 75 per cent of the animals as compared to 100 per cent of the sharp section injuries. Plantar flexion of the toes 23 per cent and 33 per cent and dorsiflexion of the foot 17 per cent and 0 per cent respectively. In neither group was there a response of dorsiflexion of the toes or fanning of the toes. After 60 days there was a 100 per cent response of plantar flexion of the toes in both groups. 77 per cent of the gunshot animals showed the response of plantar flexion of the toes as compared to 100 per cent of the sharp division experiments. Dorsiflexion of the

10 plantar flexion of the foot, followed by plantar flexion of the toes and dorsal flexion of the foot. Dorsal flexion of the toes and fanning of the toes are late signs of recovery. Normal gait and stance involve a more complicated mechanism and appear late.

11 Sensory recovery tested by the return of pain sensation over the lateral and plantar surfaces of the foot which form the area of isolated sensory supply appears 60 days after end to-end suture and 90 days after the transplantation of an autogenous graft. No critical sensory return could be found in the cases of homogenous grafts even 150 days after transplantation of the graft. The earliest response to deep pain is observed on compression of the 2nd toes 30 days after end to-end suture and 90 days after repair by autogenous grafts.

12 Muscular contractures are more often seen in animals with homogenous grafts than in animals with autogenous grafts or end to-end sutures. They occur during the stage of complete denervation as a result of the bad position assumed by the paralyzed extremity. The most common contractures involve the dorsiflexors of the foot and toes and the plantar flexors of the toes. Signs of motor recovery are observed in the contracted muscles as well as in the normal ones.

13 Trophic disturbances of the skin of the foot and toe pads and the claws are found in all the paralyzed extremities; their recovery is very slow. Trophic ulcers of the heel are present in 33 per cent of the animals after end to-end suture, 62 per cent after transplantation of an autogenous graft and 12 per cent following repair by homogenous graft. They develop during the period of denervation of the skin area during the 30th and 45th day after nerve repair. They show poor healing tendencies.

14 Reflexes such as the step and the fanning reflex are very late signs of recovery and are rarely seen even 30 months after nerve repair.

15 Response to direct electrical stimulation of the repaired nerve is the most constant and earliest objective sign of motor recovery. It begins earlier and remains better in nerves repaired by end to-end suture than by autogenous or homogenous grafts. Plantar flexion of the foot is obtained 45 days after end to-end suture and plantar flexion of the toes and dorsiflexion of the foot 60 days after end to-end suture, 75 days after transplantation of an autogenous graft and 120 days after transplantation of an homogenous graft. Excellent muscle contractions could be obtained with a threshold current of 0.1 volt in most of the animals which did not show any or little return of function when tested by other methods. The difference in degree and kind of response to electrical stimulation and other clinical tests between the nerves repaired by end to-end suture, autogenous and homogenous grafts is probably due to the heteromorphous type of neurotization which follows the more complicated structures which prevail at the suture lines and in the grafts.

16 In gunshot wounds functional recovery as expressed by return of motion, return of sensation and muscular response to direct electrical stimulation of the nerve was delayed following repair of the nerve by end to-end suture. The extensive traumatic damage which takes place for some distance around the site of trauma and the resulting heteromorphous neurotization are responsible for the functional delay. No appreciable differences are present in the rate of recovery following the implantation of a homogenous graft in gunshot or sharp surgical wounds.

17 Clinical and experimental observations warrant that the operation of choice in cases of repair of an injured peripheral nerve in man where direct end to-end suture cannot be performed is the transplantation of a nerve graft. The most satisfactory results are to be obtained by the use of autogenous grafts. If those are not available the use of an homogenous nerve transplant is justified.

THE SPREAD OF UTERINE AND OVARIAN CARCINOMA WITH SPECIAL REFERENCE TO THE RÔLE OF THE FALLOPIAN TUBE

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SINCE the sixteenth century when Gabriello Fallopio gave the first clear description of the tubes that have come to bear his name many years of observation have shown that the normal contractions of their muscular coat and the action of the ciliae of certain cells of their mucosal lining form a current from the peritoneal cavity toward the uterine cavity. This current may be reversed under certain conditions. With this knowledge at hand it is strange that relatively little has been written on the transmission of carcinomatous cells by the lumen of the fallopian tube. It is known that uterine carcinoma sometimes involves the ovaries by means other than by direct extension and that malignant lesions of the ovary spread to the endometrium by equally obscure pathways. The purpose of this paper is to report the study of carcinoma arising in the ovaries or endometrium with reference to spread by way of the fallopian tube.

The rôle that the fallopian tube has played in the spread of carcinoma of the ovary to the uterine fundus and conversely in the transmission of carcinoma of the endometrium to the ovary has long been a point of controversy. Reichel in 1888 reported 2 cases of primary carcinoma of the ovary with metastatic involvement of the endometrium. He expressed the opinion that the involvement of the endometrium was due to transmission of viable carcinomatous cells through the lumen of the fallopian tubes. Separate reports of free carcinomatous cells in the lumen of the fallopian tubes later were made by von Franqué, Monnaga, Sitzenfrey, Glendining, Clark and Norris, Schiller, Sampson (23) and Wallis.

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Abridgement of thesis by Dr. Lynch in partial fulfillment of requirements for the degree of M.S. in Surgery (University of Minnesota, 1943).

It is interesting to note that in many tests the advisability of performing curettage of the uterus, followed by implantation of radium in cases of carcinoma of the uterine fundus, is questioned because of the danger of disseminating carcinomatous cells through the fallopian tubes. This possibility of a retrograde flow has long been recognized. In 1924, Sampson (21) published the first of a series of reports in which he expressed the opinion that carcinomatous implants on the endometrium, mucosa of the fallopian tube, and serosa of the ovary had occurred as the result of transmission of viable cells by the aforementioned route.

Novak reviewed 147 cases of adenocarcinoma of the uterus and found 7 cases in which there was involvement of one or both ovaries. In 3 of these cases there also was tubal involvement. He found that the lymphatics had been invaded by malignant cells in all of the 7 cases and felt accordingly that lymphatic permeation rather than transmission through the tubal lumen accounted for the metastasis. In his review of the cases reported by Sampson he expressed the opinion that in some instances the proof of luminal spread was not adequate.

Many other reports have cited the concomitant finding of carcinoma of the ovary and the uterus, and some of the reports have mentioned tubal involvement (22-24). Glendining, Boxer, Cameron, Norris and Murphy (15), Bernstein, Werner, Offutt, Norris and Vogt (16) and Robinson have all observed one or more combined lesions in which the ovarian was thought to be the primary one. Norris and Vogt (16), Lynch, Cullen, Meigs, Crile, Offutt, Norris and Dunne (14), Smith, and Stacy have reported cases in which carcinoma arose in the fundus of the uterus and metastasized to one or both ovaries. In many

instances it also involved the fallopian tubes. Most of the authors expressed the opinion that extension had taken place primarily through the lymphatics

MATERIAL

This paper is based on a study of 113 cases of carcinoma of the uterus or ovary, or of both of these organs that were observed at the Mayo Clinic in 11½ years, namely from January 1, 1929 to June 30, 1940 inclusive. This series does not include all cases of carcinoma of these organs that were observed at the clinic in this period; it includes only those cases in which operation was performed for removal of carcinoma of one or both of these organs and in which it was possible to study in a satisfactory manner the spread of carcinoma from the uterus to the ovary or from the ovary to the uterus.¹

The 113 cases were divided into four groups. The criteria for this division will be considered subsequently.

METHOD OF STUDY

In studying this series of cases the histories were first reviewed. The pathologic specimens then were examined grossly. Representative blocks of tissue next were cut from the endometrium, the ovaries and the fallopian tubes. These blocks were embedded in paraffin, sectioned in the usual manner and stained routinely with hematoxylin and eosin and by the Galantha method for mucin.

FINDINGS

Group 1 This group includes 51 cases in which the carcinoma originated in one or both ovaries and metastasized to the fallopian tube but did not involve the endometrium. This is the largest of the four groups. It includes 45 per cent of the entire series of cases and 13 per cent of the cases in which the carcinoma originated in one or both ovaries. This is not surprising as the ovaries and fallopian tubes ordinarily are in close proximity and have common lymph channels. In many instances the carcinoma spread by means of adhesive bands.

¹In so far as it is possible examples of primary carcinoma of the fallopian tubes were deleted.

The average age of the patients was 44.7 years with extremes of 27 and 78 years. Ninety per cent of the women had been married but only 57 per cent of these had borne any children. Symptoms complained of varied in duration from 5 days to 4 years and included vaginal discharge, pelvic pain and pelvic tumor. None of the symptoms were pathognomonic of the underlying disorder although in approximately 10 per cent of the cases the presence of a bloody postmenopausal discharge seemed to be most easily explained by carcinomatous invasion of the fallopian tubes.

Bilateral ovarian carcinomas were present in 6, per cent of the cases and in the majority of instances the grade of malignancy as determined by the method of Broders was high. In all except one instance the tubal extension was homolateral. In several instances tubal spread appeared to obtain on the basis of serosal implantation. In all other cases mural involvement was by direct extension or through permeation of lymph channels. No undoubted instance was found in which mucosal implantation alone obtained and in no instance were clumps of carcinoma cells found lying free in the lumen of the fallopian tube.

Group 2 This group includes cases of carcinoma of the uterine fundus with involvement of the fallopian tube (or tubes) but without metastasis to the ovaries. Twelve cases or 3.2 per cent of the cases of primary uterine carcinomas studied fulfilled the criteria established for this group. The average age of patients was 53.5 years, slightly lower than the usual figure cited in the literature for patients with carcinoma of the fundus. Extremes of 30 and 72 years were noted. Ninety per cent of the patients were married and the incidence of fertility was 90 per cent.

Symptoms were of the type to be expected in carcinoma of the uterus with no features indicative of tubal extension. Symptoms on an average had been present for slightly more than 1 year. Nine of the lesions were graded 1 or 2 (Broders method); 9 had involved the fallopian tubes bilaterally and 9 had invaded the tubal mucosa. However in all 12 cases there was evidence of submucosal permeation in the lymphatic spaces with none demon-

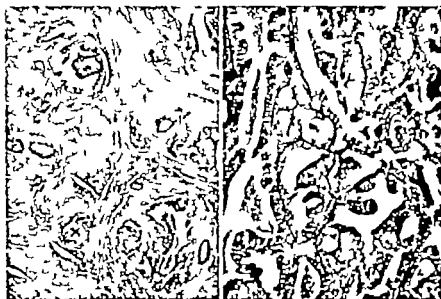


Fig. a, left. Adenocarcinoma, grade squamous epithelial elements visible (×5). b, metastatic adenocarcinoma of uterus (×65).

of uterus. mixture of glandular and squamous cell elements. section stained with hematoxylin and eosin.

strating evidence of spread via mucosal implantation exclusive of other methods.¹

Group 3. This group includes cases of carcinoma of the ovary (or ovaries) and endometrium with involvement of the fallopian tube or tubes. In 20 cases all of the aforementioned structures were involved. In 12 of these cases the primary growth was ascertained to be ovarian; in 6 it was uterine and in the remaining 2 cases no decision could be reached in this matter. The average age of patients in the group was 51.1 years with extremes of 35 and 69 years. Fifty per cent of the patients had passed the clinical menopause. Symptoms present combined the features of those in groups 1 and 2. The symptoms had been present for an average of 17 months. The symptoms were not characteristic for this group of lesions.

Pathologically the criteria used for indicating the ovary as the primary site of the malignant lesion were (1) the size, degree of encapsulation and other gross features of the ovarian tumor; (2) the presence of papillary projections and of cysts; (3) the presence of psammoma bodies; (4) the demonstration of

mucus; and (5) the finding of bottle neck cells which occasionally have caused pathologists to suspect primary involvement of the ovary in examination of malignant material curetted from the uterus. Conversely the observation of rather well differentiated uterine glands of that peculiar mixture of glandular and squamous cell elements known among pathologists as adenocarcinoma, indicated that the uterus might be the site of origin of the primary tumor (Fig. 1 a and b). Invasion of the myometrium, whether centrifugal or centripetal, was of some assistance in cases in which the site of origin of the primary tumor was doubtful. In some cases the occurrence of coexisting and independent uterine and ovarian lesions could be ruled out entirely.

All grades of malignancy were encountered; however, in general lesions that occurred primarily in the ovary were potentially more malignant than were those that occurred primarily in the uterus. Bilateral tubal involvement was present in 50 per cent of the cases in this group. Unilateral involvement was equally shared by the right and left tube and extension from tube to ovary (or vice versa) tended to be homolateral.

The site of the tubal involvement was as

¹Recently, however, a number of examples of such modes of spread have been observed by one of us (Dockerty).



Fig. 2. a, Typical papillary cystadenocarcinoma grade 2 of ovary section stained with hematoxylin and eosin ($\times 43$) b section of corresponding fallopian tube showing metastatic involvement, section stained with hematoxylin

and eosin ($\times 43$) c, metastatic papillary adenocarcinoma grade 2, of the endometrium (primary lesion was situated in the ovary) section stained with hematoxylin and eosin ($\times 43$)

follows in 11 cases the mucous muscular and serous coats were involved in 6 cases only the serous coat was involved in 1 case involvement of the muscular coat was associated with secondary ulceration of the mucosa, and in the 2 remaining cases the involvement was limited to the mucosa. With the possible exception of these 2 cases the lesion appeared to have spread by direct extension or by lymphatic permeation or by both of these methods (Fig 2 a b and c)

Group 4 This group includes 30 cases of carcinoma of the ovary (or ovaries) with concomitant carcinoma of the endometrium but without malignant lesions of the fallopian tubes. The average age of patients was 53.1 years with extremes of 41 and 70 years. Of 21 married patients 13 had borne children. Clinical menopause had occurred in 17 cases.

Symptoms complained of as in group 3 shared the features of those of uterine and of ovarian carcinoma. They were rarely characteristic of the extent, to say nothing of the exact nature of the pathologic lesions in the pelvis. The average duration of symptoms was 8.6 months.

The difficulties encountered in ascertaining the site of the primary growth were fully as

apparent as they were in group 3 and the site was comparable in both groups. In 14 cases spread by extension contiguity or lymphatic permeation accounted for the presence of identical lesions of the ovary (or ovaries) and the endometrium. In 11 cases the lumen of the fallopian tube seemed to play the part of a passive conduit for the transmission of carcinomatous cells without becoming secondarily invaded. In 4 of these 11 cases the lesions were primarily uterine. In 3 of these involvement of the ovaries took the form of surface implants and in 1 case there was invasion of a recently ruptured hemorrhagic cyst. In 7 cases a primary ovarian carcinoma spreading exclusively to the endometrium produced lesions that were diffuse in 2 instances and circumscribed and cornual in 5 cases. In all 7 cases penetration of the myometrium was minimal. In the 5 remaining cases it is quite possible that the ovarian and the endometrial lesions represented independent primary growths as their respective microscopic pictures differed somewhat.

DISCUSSION

It is the consensus as gathered from the literature that the uterus is one of the most

frequent sites of carcinoma among women. Malignant lesions of the uterine fundus account for 25 per cent of all malignant lesions of the uterus. Carcinoma of the ovaries has been found to represent 7.7 per cent of all gynecologic lesions by Norris and Murphy (15). Lynch has determined in his series of cases that 13.3 per cent of all malignant lesions of the pelvis arose primarily in the ovary. In our particular series of cases uterine (fundal) and ovarian carcinoma occurred with equal frequency. However this does not take into account the cases in which the lesion was inoperable.

The incidence of multiple malignant lesions has been variously reported. In 1933 Hurt and Broders stated that in 3.4 per cent of a series of 2124 cases the lesions were multiple. Warren and Gates (30) reviewed 1250 cases of carcinoma and found multiple lesions in 1.04 per cent of the cases. White has concluded from his studies that in about 4 per cent of all cases of malignant lesions there is more than one primary site of origin and that multiple lesion usually appear at an earlier age than do single lesions.

Offutt reported that in 8.6 per cent of 616 cases of papillary cystadenocarcinoma of the ovary the lesion was associated with carcinoma of the uterine fundus. Offutt found concomitant lesions of the ovaries in 11.9 per cent of 512 cases of malignant lesion of the uterine fundus. Holland in an examination of 10,000 fallopian tubes, found that 81 were involved by carcinoma. In 62 instances the growth was secondary to an ovarian neoplasm while in 8 the primary focus was in the endometrium. Norris (15) found 8 instances of secondary neoplastic growth in the fallopian tubes in 2,000 gynecologic specimens. In 15 per cent of 759 cases of uterine and ovarian carcinoma in our series extension was indicated by the criteria listed in the foregoing 4 groups.

Anatomic studies have demonstrated the existence of interconnecting links in the lymphatic drainage of the uterus, tubes and ovaries. It is not surprising therefore, that our studies have shown direct extension and lymphatic permeation as the chief pathways in the dissemination of carcinoma from one to

the other of the aforementioned structures. The surprisingly small number of cases which such modes of transmission do hold revolve around the following question: Does carcinoma spread by the lumen of an intact fallopian tube? Granted that it does we can explain the occurrence on the surface of an ovary of a single metastatic lesion from let us say a primary adenocarcinoma of the uterine fundus. There is evidence in the case of Kruckenberg's tumor that the ovarian peritoneum like the general peritoneum may play host to the tumor implants. Similarly in the case of ovarian carcinomas that occur among a relatively young group of patients, endometrial implants could be explained on the basis of implantation on a type of epithelium which is periodically breaking down and hence by no means intact. It is accordingly noteworthy that in very few instances was the mucosa of the fallopian tube involved by the implantation method. In almost all instances the phenomena of direct extension or lymphatic permeation or both were in operation. The inescapable conclusion is that carcinoma may spread from the uterus to the ovaries or vice versa. In the majority of cases the spread is by direct extension or by lymphatic extension or by lymphatic permeation alone or combined, and frequently with simultaneous involvement of the fallopian tube as an intermediary stage in the process. In a minority of these cases viable malignant cells may spread through the lumen of the fallopian tube, usually without becoming implanted on its mucosa.

SUMMARY

In 113 cases of operative uterine and ovarian carcinoma the malignant process has invaded other pelvic structures. In 51 or 45 per cent, of the cases the lesion arose in the ovary and involved the fallopian tube and in 12 cases it arose primarily in the fundus of the uterus and involved a fallopian tube. In 30 or 18 per cent, of the cases the lesion involved the ovaries, endometrium and tubes. In 12 of these cases the primary site of the lesion was in the ovary, in 6 cases it was in the uterine fundus and in 2 cases the primary site was doubtful. In 30 cases ovarian and endometrial

carcinoma coexisted without evidence of tubal lesion. The primary growth was uterine in 12 cases and ovarian in 13. In 5 cases the site of the primary lesion was doubtful and the possibility of two independent sites of origin could not be excluded entirely.

Approximately 6 per cent of ovarian carcinomas metastasized to the endometrium and examination of curetted material occasionally revealed the extrauterine site of the primary growth. Conversely about 4 per cent of operable carcinomas of the uterine fundus eventually involved the ovary or ovaries. In both circumstances the fallopian tube seemed to act as the intermediary host to the malignant cells. In only 1.4 per cent of cases did it serve in the capacity of a passive conduit, and in only 0.4 per cent was the direction of the flow reversed, namely from uterus to ovary. From a practical standpoint therefore little risk was indicated for the production of ovarian or abdominal implantation in curetting a uterus which is the site of a malignant lesion prior to the insertion of radium. In only a few cases was evidence found that carcinoma cells became implanted on tubal mucosa in the extension of malignant lesions of the ovary or fundus of the uterus.

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THE EFFECT OF CONTINUOUS CAUDAL ANALGESIA UPON UTERINE MOTILITY DURING LABOR

A Study of Fifty Patients with the Lóránd Tocograph

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THE rapidly extending employment of continuous caudal analgesia in obstetrics has necessitated a closer study of the effect of this method, not only on mother and infant but also upon the motility of the uterus. Opinion on this latter point is divided.

Both Greedy and Hesselstine and Lorhan, state "The uterus appears not to relax, and appears to maintain its normal motility and mechanism."

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To determine more accurately the effect of caudal analgesia upon the uterine contractions, the labors of 50 patients under caudal analgesia were studied by means of the Lóránd tocograph an instrument devised for recording graphically the contractions of the uterus through the anterior abdominal wall (10-12).

METHODS AND MATERIALS

The records of uterine activity under caudal analgesia were made between November 8, 1943 and April 8, 1944, upon 50 women in labor from the ward services of the Philadelphia General Hospital and the Kensington Hospital for Women, Philadelphia. The observations were recorded with the Lóránd tocograph. The closed circuit needle technique, as originally described by Hingson and Edwards (3) was used throughout. The anesthetic agent was metycaine 1.5 per cent in Ringer's solution.

From the Obstetrical Services, Philadelphia General Hospital and Kensington Hospital for Women. Thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania, toward the requirements for the degree of Master of Medical Science (M. Sc. (Med.)) for graduate work in Obstetrics and Gynecology.

After a 15 minute control period of recording and without removing the tocograph the analgesic dose of metycaine was administered. The tocograph record was usually continued for a hour or more after complete analgesia was obtained. In each instance the level of analgesia was carefully checked. The level of analgesia was considered to be high when it went to the 4th thoracic segment or higher.

In midthoracic block the level of analgesia was below the 4th thoracic segment and above the 11th thoracic segment with complete relief from the pain of uterine contractions.

Low caudal block existed when the analgesia did not extend high enough to relieve the pain of uterine contractions but involved sacral and lower segments only.

RESULTS

The tracings obtained from 50 patients in labor were evaluated according to the effect of the analgesia upon the strength and frequency of uterine contractions and on the uterine tone.

Contractions. Of these patients 33 demonstrated no significant change in either strength or frequency of contractions (Fig. 1). In 9 patients the contractions were interrupted for periods of 30 minutes to 2 hours (Fig. 2).

Six patients exhibited a decrease in frequency of contractions, and 1 a noticeable decrease in the strength of the contractions (Figs. 3 and 4).

Two patients showed significant improvement in both the strength and frequency of contractions (Fig. 5).

Tone. Of the 50 patients studied 27 showed no change in uterine tone during analgesia. However 22 patients exhibited a progressive decrease in tone, and 1 exhibited a marked rise in tone (Figs. 6 and 7).

OBSERVATIONS

Analysis of the results obtained in this study indicate that the most important factor influencing the motility of the uterus under caudal analgesia was the height to which the analgesic level was permitted to ascend.

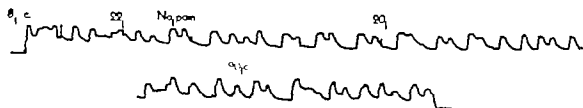


Fig. 1. This record is typical of the 33 patients in whom labor continued without change in strength or frequency of contractions. Complete relief from pain was attained at the position marked "No pain."

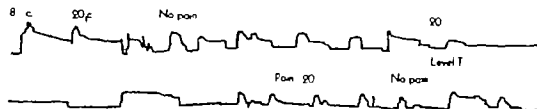


Fig. 2. Illustrated interruption of uterine contractions for 40 minutes when level of analgesia was permitted to ascend to the level of the second thoracic segment. Note absence of contractions when level reached T₂ and spontaneous return of contractions when level fell to symphysis pubis.

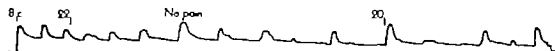


Fig. 3. The progressively increased interval between uterine contractions may be observed. Six patients exhibited similar mild decrease in the frequency of contractions.

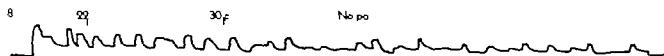


Fig. 4. This patient exhibited a noteworthy decrease in the strength of uterine contractions. Note the smaller amplitude of the later contractions as compared with those in the control period.

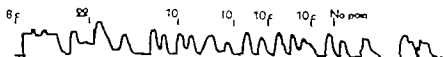


Fig. 5. Marked increase in strength of uterine contractions observed under low caudal block. Note tiny contractions of the control period. Also 4 additional doses were required to raise analgesic level and relieve pain.

Each of the 9 patients in whom labor was interrupted had a level of analgesia above the 4th thoracic segment. When the level was allowed to fall, labor started again.

The 2 patients in whom contractions were increased in strength had levels of analgesia involving the sacral segments only. These women complained that the pains were made worse and the tocograph records showed significant increase in the strength of the uterine contractions. When the analgesic level was subsequently raised above the 11th thoracic segment and the pain relieved the stronger pattern of contractions persisted.

In 35 patients levels of analgesia between the 6th and 7th thoracic segments were attained. Of these patients 7 recorded minor changes in the strength or frequency of contractions. These changes were not sufficient appreciably to lengthen

the labor. The remainder of these patients recorded no change.

The remaining 4 patients numbered those in whom labor was not interrupted even though the analgesic levels were above the 4th thoracic segment (Fig. 8).

That labor may often be interrupted by analgesia above the 4th thoracic segment of the cord would seem to indicate that the motor fibers to the uterus leave the cord in this area. This is in accord with the findings of Cleland and of DeLee who observed that the motility of the pregnant uterus was not interfered with even after transection of the cord at the level of the 6th thoracic segment.

Hingson (8) has used this principle in the management of 4 patients with premature labor induced by accidental trauma. High caudal block

THE EFFECT OF CONTINUOUS CAUDAL ANALGESIA UPON UTERINE MOTILITY DURING LABOR

A Study of Fifty Patients with the Lóránd Tocograph

DONALD S. FRANKEL, M.D., Philadelphia, Pennsylvania

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PILONIDAL CYST AND SINUS THEIR MANAGEMENT AND OPERATIVE TREATMENT

WILLARD BARTLETT Jr M D F.A.C.S Commander MC U.S.N.R. St. Louis, Missouri

THE prevalence of pilonidal cyst and sinus has been repeatedly brought to the attention of the medical officers in the armed services and various phases of military life have been charged with precipitating activity inflammation and infection in these lesions. Authors for the most part, have tabulated formidable numbers of postoperative sick days in their individual series many of them presenting 35 sick days or more per case and there are numerous instances of patients still being unhealed as long as 100 days after operation. Failure to obtain primary union regularly after suture of the wound is reported and largely for this reason various efforts to achieve some compromise with what is admittedly the ideal of primary closure have been formulated. A measure frequently recommended is closure of the skin margins to the sacrococcygeal fascia after complete excision of the lesion and its surrounding bed of fat. Another method that has its advocates is the removal of only the most superficial portion of the cyst and the marsupialization of the remainder by suture of its margins to the skin in the expectation that the exteriorized cyst wall will assume the characteristics of normal skin.

The length of time which must elapse before a patient can return to full duty after these procedures is still far greater than in those in whom primary union has been achieved. If they are to be adopted as routine measures it is as suitable for the average case in the young men who make up the overwhelming majority of the patients reported it is necessary to assume (1) that there is no practicable alternative to prolonged disability in order to assure cure (2) that the final result will be satisfactory in a high percentage of cases after

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such procedures and (3) that excision and primary suture while ideal, cannot be accomplished with great regularity. It is the writer's belief that none of these assumptions can be safely made and his own experiences with such lesions in 38 consecutive admissions over a recent period of 18 months are offered here with substantiation of that opinion. Personal conversation with other surgeons in both of the armed services and observation of their patients convince the writer that his results are in no way unusual.¹ The fundamental principles on which those of us who have routinely practiced primary closure after excision are agreed are presented for consideration together with an outline of points of management and operative technique. It is only fair to state as have all other authors presenting data on such operations on military and naval personnel that the final results in respect to recurrence will rarely become known to the operator himself. It can reasonably be expected however that the application of a given method to military personnel should yield substantially the same recurrence rate as that formerly encountered in civilian practice unless the average lesion in the former prove to be more severe. In the experience of the writer the reverse has been true seriously complicated cases being less common in these relatively young patients than among civilians applying for surgical treatment.

PERSONAL CASES

There was a total of 38 admissions to the sick list involving 34 patients with the diagnosis of cyst teratoma, sacrococcygeal in a period of 18 months. (The incidence is interesting in relation to the total of operative cases

¹As these results were being tabulated, a paper by Ralph V. Byrne, Lieutenant Commander M.C., U.S.N.R., appeared in the *U. S. Naval Medical Bulletin*, 644, 4: 386-389. It reports excision and complete suture in 20 of 3 patients, with primary healing in 7. The average healing time was 6 days, the longest being 30 days. The author's views, in general, are almost identical with those developed in the present publication.

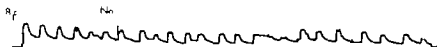


Fig. 6. Note that the record runs progressively downward. This represents fall in uterine tone which occurred

in 2 patients. The significance of the decrease in uterine tone is as yet unexplained.

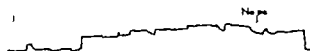


Fig. 7. The record of one patient with an unexplained rise in tone. It should be noted as possibly significant

that the rise in tone occurred when only low caudal block was attained and before complete relief from pain.

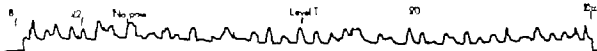


Fig. 8. The record of one of 4 patients is presented in whom a level of analgesia above the 4th thoracic segment

was attained without causing interruption of uterine contractions.

was maintained for about 12 hours during and following which there was complete cessation of labor. Three of these patients went on to term; the fourth went 3 weeks past term, and all were delivered of normal babies.

Four patients received high caudal block above the 4th thoracic segment without noticeable change in their labor. This is not explained adequately. The varying thickness of myelin sheaths in different nerves and individuals as shown by several observers (4, 6, 7) may be a factor.

Two patients in whom sacral block only was attained showed increased labor. This might indicate that the parasympathetic fibers of the sacral nerves, in addition to their function of maintaining the tone of the smooth muscle of the cervix, may have an additional function of inhibition of the remaining uterine musculature. Removal of this inhibitory influence may account for the improvement in labor.

The significance of the diminution of tone observed in 44 per cent of patients studied is not explained. However clinically it does not appear to be equivalent to the relaxation of the uterus produced by deep ether or chloroform anesthesia considered necessary for intrauterine manipulations such as podalic version or decomposition of frank breech. We do not believe it sufficient to relax a contraction ring.

SUMMARY AND CONCLUSIONS

A Lóránd tocograph was used to record graphically the labors of 50 women receiving continuous caudal analgesia.

The most important factor determining the effect upon the uterine motility was the level to which the analgesia ascended.

When the recommended level (between the 6th and 10th thoracic segments) was maintained, only 20 per cent showed any decrease in uterine motility and these were very minor changes. The remainder were unaffected.

When the level of analgesia was permitted to ascend above the 4th thoracic segment, 69 per cent of the patients had their labors interrupted.

When a low level of analgesia involving only the sacral nerves was achieved in 2 patients there was a marked improvement in the strength and frequency of the uterine contractions. This improvement continued after relief from pain was attained.

Forty four per cent of patients studied showed a progressive decrease in uterine tone. This did not appear related to the level of analgesia.

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Among the 22 cases in which excision was done there was one with a shallow (2 cm) sinus persisting some 11 weeks after excision *en bloc* of skin, fat, and fascia and primary closure by the writer the only known recurrence in this series. Excision *en bloc* through double elliptical incision of skin, fat and sacrococcygeal fascia was the technique employed in 7 instances. These were among the earliest cases in this series and followed the previous custom of the writer in civilian practice. Routine section of these blocks of tissue operated on in a quiescent phase however, revealed the characteristic lesion to be a surprisingly small cyst 2 to 3 centimeters long in its greatest diameter invariably superficial to the fascia and rarely having secondary sinuses.

On the basis of these observations it seemed obvious that a wholly unwarranted sacrifice of normal tissue, with consequent difficulty of closure, was being made by the employment of block dissection in the average case even though an incision only some 6 to 8 centimeters long and of a maximum width determined by the palpable margins of the cyst was used. It was decided to continue to define the lateral margins of the cyst at their attachment to the skin then to follow the cyst wall by dissection removing only such skin and fat cephalad and caudad to the lesion as was necessary to outline a skin incision of the necessary length in proportion to width for easy closure. This would result in the sacrifice of only a few millimeters of fat lateral to the cyst and to a depth of less than 1 centimeter elsewhere. It would be necessary of course to distinguish among strands of tissues of three types during such an enucleation excision any of which may be seen to blend with the fibrous capsule about the cyst wall (1) blood vessels (2) fibrous tissue reflections of the sacrococcygeal fascia, (3) epithelium lined tracts. It is the writer's contention that the surgeon operating upon such cysts in a quiescent phase should be able to make this gross differentiation. Such was the technique employed in the 14 operations listed as enucleation excision.

The validity of these observations and assumptions was borne out by the finding of

secondary sinuses in only 2 of the 21 patients subjected to primary excision, in only one of them was the wound packed open to await healing by granulation. Fibrous strands were occasionally followed down through the fascia particularly along the coccyx, and the cyst was rarely as large as the end of one's thumb. Primary closure in layers without tension and without the necessity for the mobilization of fat was relatively simple except when the cyst lay rather high in the sacral region where the fat pad is thinner than elsewhere. These patients may be fairly regarded as being an average run-of-the-mill group as they are seen in the young men of the armed services.

A point of technique that the writer has not seen advocated is the incision of the skin obliquely rather than at right angles to its plane throughout the length of the incision in order to assure perfect coaptation of skin edges in closure during which both margins of the wound are rolled toward the midline with resulting inversion of the skin if the latter is incised at right angles to its surface. Closure of the fat not only from side to side but with attachment by suture to the fascia is essential to the obliteration of dead space. The writer prefers suture of the fat by one or two rows of fine material of whatever nature to its closure with the skin by through and through sutures. A small soft rubber drain was placed to the depth of the wound in 13 of the 20 patients in whom primary suture was done and was removed on the first day after operation in 8 of these. Only a wound of this region in which hemostasis is literally perfect should be left undrained. Since all excisions were done under circular (field) block analgesia with 2 per cent procaine the risk of delayed bleeding though minor in amount seemed to make this precaution against hematoma formation worthwhile. This type of analgesia is ideal though time consuming as no distortion of the tissues in the operative field occurs as would be the case with infiltration. There is no objection to the use of spinal analgesia for this purpose. The wound surface was usually 'frosted' very lightly with crystalline sulfanilamide before closure of the wound was carried out and a compression dressing was applied routinely.

for this period to be reported later number ing slightly over 500.) Of the 38 admissions, inflammation was present in 24 cases and absent in 14.

The term inflammation has been applied rather than infection in this compilation only because the former is in accord with the system of nomenclature of the Medical Department of the Navy. The great majority of the 19 patients presenting acute inflammation had frank abscesses in the cyst which had perforated the deep layers of the skin on admission and had, in a few cases established inadequate drainage. Of the 14 patients who were treated by incision this operation was done within 24 hours of admission and the quantity of pus was estimated to be 1 ounce or more in 9 instances. Organisms in abundance were invariably present in stained preparations of direct smears. The only patient not operated on was a straggler who had established adequate drainage spontaneously and whose inflammation was subsiding on admission. He refused excision after 5 days of treatment and was sent on to his own activity to await disciplinary action and eventual excision of the cyst. In 4 patients the acuity of the inflammation was so early or began to subside so promptly after admission that excision of the lesion was done in from 1 to 8 days.

Of the 5 patients showing chronic inflammation and purulent discharge on admission 3 had not been free of discharge for longer than a week at a time for over 10 months. Treatment to minimize infection and decrease drainage was carried out for a maximum of 6 days before excision. One patient showed moderate local improvement on treatment for 12 days, but a generalized pyoderma which had developed after incomplete excision elsewhere of his cyst some 3 months previously proved to be so indolent that he was transferred to a naval hospital for further treatment.

Of the 14 admissions (13 patients) without current inflammation there was a past history of acute inflammation in 12. In 7 cases incision had been done on from 1 to 4 occasions it had been carried out at our activity in 3 cases. One patient was a readmission with a small sinus persisting after excision 10 weeks previously by the writer. Excision of the

lesion was done within 2 days of admission in all these cases.

It should be clear from this presentation of the past history and condition on admission that no asymptomatic cysts or blind sinuses were operated upon. All of the patients had lesions which were, or had been, incapacitating. A history of previous incision on from 1 to 4 occasions was given by 14 of the patients. It was impossible to decide in view of these instances an effort at excision had been made.

Further comment on the 14 patients to whom incision was done on admission is pertinent. Incision was performed on the day of admission in 10 instances, on the following day in the remainder. Sulfathiazole, 5 grains by mouth daily, was started on admission and continued for the few days that the patient remained on the sick list. The decision to leave a soft rubber drain in the incision was made on the basis of the size of the cavity and its depth. Even though pus was under pressure in all these cases an effort was made to express all the free necrotic material at operation the wound being spread open by a bone spat and all hair and semisolid material wiped out. The tendency was increasingly toward the use of an incision between 2 and 3 centimeters in length in order to obtain prompt evacuation of the contents of the abscess rather than the use of a small stab wound which would serve only to relieve tension. The drain was removed in from 1 to 3 days, by which time the discharge was small in amount and largely serous in nature. It was not necessary to reopen any of the wounds. Three of these patients were subsequently readmitted for excision. A circular block analgesia of the full thickness of the skin was employed in nearly all cases. The common practice of using ethyl chloride spray for topical analgesia has been long since abandoned by the writer as being inadequate to permit the procedures outlined here. The problem is not at all the same as that involved in draining a furuncle. If all foreign material particularly hair is not removed at the time of incision these wounds will continue to drain intermittently and remain inflamed for months. The avoidance of a foreign body reaction permits prompt heal-

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Primary healing was obtained in 18 of the 20 cases in which complete suture of the wound was done. The 1 partial failure occurred in a patient in whom excision of a large cyst located higher on the sacrum than usual was performed on the 6th day of treatment, earlier than would have been ideal in view of the considerable induration about the cyst and the profuse purulent discharge from 2 of his 4 midline sinuses on admission. Incision had been made elsewhere 10 months previously and drainage had been almost continuous thereafter. The field was still too vascular due to lingering inflammation for good hemostasis at the time of operation and there was sufficient induration of the tissues to make approximation difficult even after mobilization of the fat layer. The comment was made that the choice between packing the wound and attempting closure was probably an even one. A hematoma in the lower third of the wound was drained on the 4th day and mild wound infection supervened, yet the upper two-thirds of the closure held securely and healing of the lower third by secondary intention was complete on the 31st day—a decided saving of time over what could have been expected had no closure been attempted. The occurrence of a persistent, superficial sinus in one other case with eventual reoperation has been referred to.

Patients were discharged under treatment on an average of 4 days after simple incision with a recommendation for light duty for a period of one week. If at the end of this period of light duty the man was to be transferred to another activity the recommendation was made that excision of the lesion be done after a further interval of 6 to 8 weeks. The usual immediately postoperative care involved sulfonamides orally as previously noted, local heat and sitz baths twice daily following removal of the drain until the wound was free of discharge, ordinarily on the 4th day. No probing or other exploration of these wounds was done. It was not necessary to extend the period of light duty in any case. Three of these patients returned for excision of the lesion at intervals of less than 10 weeks. None had had pain or discharge in the interim. An interval of perhaps 6 weeks between in-

cision of a grossly infected cyst and its excision is ideal, though frequently not practicable. When the interval is less than 3 weeks, the remaining induration and increased vascularity make both accurate dissection and closure noticeably more difficult and healing is impaired.

The longest period to complete healing in the 22 patients whose lesions were excised was 43 days. This patient in point was the only one for primary excision in whom packing of the wound was employed. The other patient in whom closure was not made has been previously referred to. He was completely healed in 10 days after secondary excision of a small, persistent sinus. The second longest interval between operation and healing, 31 days, has also been alluded to as occurring in the other patient in whom complete primary suture was partially unsuccessful. All other patients were discharged from the sick list completely healed and fit for duty in 15 days or less after excision, the average being 12.7 days. No recommendation for light duty was made in these cases.

Postoperative infection was not a factor of consequence in this series of patients. In only 2 patients was purulent drainage from the wound present after excision, though slight redness about the skin sutures was not uncommonly seen. The postoperative regimen followed with rare exception in these patients involved (1) a minimum of 10 days strict confinement to bed, (2) the avoidance of lying on the back during this period, (3) clear liquid diet and paregoric for 3 days after operation and a low residue diet and mineral oil daily thereafter, (4) the administration of pituitrin to induce the first bowel movement on the 4th or 5th postoperative day and the avoidance of an enema at any time, (5) the institution of oral sulfathiazole therapy, 5 grams daily if redness developed about the sutures, (6) careful regular cleansing of the wound area, gluteal cleft, and perianal skin to maintain dryness of these tissues. Alternate skin sutures were usually removed on the 7th day, the remainder on the 9th or 10th day. Sutures about which there was slight necrosis were not removed before the 10th day but were allowed to cut through the tissues. The buttocks were kept strapped together lightly

for 10 days and healing of the incision per primam was almost invariably complete at this time. Incidentally it is a common paradox to find that the surgeon has strapped the patient's buttocks together but has maintained the patient in the supine position. The two measures as explained produce mutually antagonistic effects on the wound. A few days of increasing activity after being allowed out of bed was sufficient for the necessary regaining of strength particularly of the legs in these young men before they were returned to duty. The opportunity of shore liberty was a powerful incentive to complete recovery.

The writer regards the practice of allowing these patients to be ambulatory before the 10th postoperative day as an invitation to wound complications regardless of the suture material used and the method of its insertion. If one will have a patient who already has a disruption of the lower end of his wound sit on a stool inspection of the wound in this posture will reveal that the defect has assumed a greater dimension transversely than vertically and any posture that tends to flatten the buttocks exerts a disruptive stress on the incision. Even though buried sutures be not actually broken or pulled out of the tissues such a stress can only tend to form dead space in the wound with subsequent serum collection. The early removal of skin sutures leaves the skin itself without any strength to resist separation and if through and through sutures are depended on for closure only a plastic exudate holds the entire wound together for the first 10 days if the sutures are removed before true fibrous tissue is laid down in healing. These are simple fundamentals of wound healing which apply to any wound that tends to burst on stress rather than to close itself as in the case of a muscle splitting incision. The writer has seen these principles violated repeatedly with predictably poor results. In this particular operative field all the tissues are normally under tension and excision of these layers inevitably increases the tension on all layers after suture. Dead space once formed is rapidly filled with serum and if it does not break through the superficial closure before the patient is dismissed from medical observation it remains more or less encapsu-

lated and acquires a chronic granulation tissue base. Breaking down of the wound weeks after discharge from the sick list may then occur and the lesion is improperly labelled a recurrence with the implication that some portion of the cyst or sinus had not been excised.

Personal inspection of a few patients who have had a partial closure by the compromise method of suture of skin margins to the sacro-coccygeal fascia leaving a space between to granulate in the hope of eventual epithelization has revealed unsatisfactory late results although all of the patients examined had been returned to a duty status on the assumption that they were fit for duty. They were usually still unhealed after months on the sick list and all complained of pain on sitting. This procedure disregards the fundamental necessity for a scar of normal thickness to cover the sacrum, a necessity familiar to all who have had experience with posterior resection of the rectum by the Kraske method. Suture of the skin margins to the fascia leaving the intervening space free of fat precludes the possibility of any but a thin scar. With due regard for the fact that these patients who still complain of pain and tenderness become labelled as gross exaggerators after 3 or 4 months all previous surgical experience indicates that they will be made comfortable by a plastic procedure which involves mobilizing a pad of fat and skin over the sacrum. Fat is perhaps sacrificed at even greater cost than skin in this region.

The writer has not had the opportunity of examining patients after the marsupialization procedure previously referred to but is not aware of the validity of the evidence for the claim made that the remaining portion of cyst wall will assume the characteristics of skin. Finally laying open sinuses and cysts that have given symptoms from nearly all of which micro-organisms can be cultured as a preliminary to excision makes closure hazardous due to the likelihood of contamination of the field. There is a coincidence between advocacy of such preliminary exploration of the cyst and of a compromise with the ideal of primary closure which suggests that this risk has been widely appreciated. Marsupialization does in fact offer a means of removing

some portion of an inflamed cyst rather than simply draining the abscess but that it has any place as a routine procedure for the average case is by no means clear from the published data. The length of time reported per case is in excess of that following successful primary closure and the assurance of a comfortable dry scar as a final result awaits the publication of late observations on these patients.

SUMMARY

Recently published experiences with excision and primary suture for pilonidal cyst and sinus indicate considerable dissatisfaction with the results, although it is generally agreed that this is the ideal procedure.

Various substitute measures which compromise with either complete excision or complete closure of the wound have been advocated as routine operations. They involve however a prolonged period of healing and uncertainty of ultimate result the reasons for which have been discussed.

The writer believes that the average severity of the lesion as seen in members of the armed forces is less than that usually encountered in civilian practice and he has continued to use complete excision and primary suture as the routine procedure unless a frank abscess is present. Analysis of his operative cases over a recent 18 month period reveals an average of less than 15 postoperative sick days for the 22 patients in whom excision was done. Complete closure of the wound in 20 patients and the achievement of primary union in 18 of these with less than 13 sick days per case after operation.

Enucleation excision removing a minimum of healthy tissue has been done in a majority of the cases rather than excision *en bloc* and contributes importantly to the ease with which the wound may be closed.

Fundamental considerations of management and technique are presented as essential to achieving an ideal result in a reasonable percentage of cases.

MULTIPLE CARCINOMAS OF THE LARGE INTESTINE

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WHILE multiple cancers of different or of paired organs are no longer looked upon as biological curiosities multiple malignant tumors of the large intestine have been reported infrequently. This subject presents many interesting controversial aspects particularly with reference to cancer immunity longevity and origin. There are many reports on synchronous and metachronous cancers in different organs but the literature is sparse in its treatment of multiple carcinomas limited to the large intestine. The multiplicity of malignant lesions in this location presents problems of diagnosis and treatment that differ from dual lesions elsewhere. This investigation is limited to cancers in the colon and rectum as encountered during the years 1934 to 1943 inclusive.

IMMUNITY AND MULTIPLE CARCINOMAS

Caylord Clowes and Baeslack in 1905 noted that in animals inoculated with the Jensen rat tumor regression frequently occurred. Once recovery took place these animals were insusceptible of reinoculation. These observations were corroborated by Michaels Borrel and Ehrlich and led to the theory that active immunity could be established by the inoculation of tumor tissue. It was soon apparent that such resistance while most pronounced against the specific tumor used extended to other growths to a lesser degree. Ehrlich broadened the theory considerably by concluding that resistance thus produced was universal (pan immunity).

Based on experimental transplantation of malignant cell in mice he stated that one cancer furnished immunity to the subject against any additional primary cancer. This immunity may be acquired or natural. Although one group of mice may be resistant at

all times to transplantation of a specific tumor tissue others at first may be resistant. With repeated applications successful takes eventually can be obtained. If the mouse with a successful transplant can overcome the growth or if the tumor tissue be removed a permanent immunity may be established in that mouse against further inoculations of that same specific tumor tissue. Maud Slye was never able to induce cancer in mice resistant by heredity. In mice susceptible to cancer in a specific location she was never able to produce a malignant growth in other areas in spite of repeated trauma. Boyd maintained a similar view that immunity against the appearance of a second cancer is conferred on the subject by the presence of a malignant neoplasm. For this reason he stated that multiple cancers are very rare.

Iwing believed that the presence of more than one carcinoma in the same or in different organs of the same patient was nothing more than the accidental coincidence in several organs of the biological factors in the genesis of tumors. Fried found only one case of multiple cancer in one thousand autopsies. Hanlon and Orr agreed that their occurrence is only coincidence.

Teller by artificial production of easily curable and harmless skin cancer claimed to have created immunization against visceral cancer. Confirmation of his work was advanced by Schmidt who in a study of multiple malignancies based on thirty seven hundred consecutive necropsies did not find a single visceral cancer combined with a skin epithelioma. However he concluded that it would be wasteful thinking to a time that in order to prevent visceral carcinoma one needs only to acquire artificially an easily curable skin malignant lesion.

In the experimental laboratory Berson and Weinman found that in a group of mice infected in mice between the presence of a malignant tumor in one organ and the appearance of a second cancer in another.

TABLE I.—AVERAGE AGE IN SINGLE CARCINOMA OF THE LARGE INTESTINE (1934-1943 INCLUSIVE)

	Male	Female	Total
Colon	8	7	20
Rectum	105	8	8
Total	85	59	344
Percentage	31.8	6	100

Average age—56 years

LONGEVITY AND MULTIPLE CARCINOMAS

The belief was held by several investigators (Hanlon Orr) that, as a result of earlier diagnosis and treatment the survival period after the removal of a cancer permitted more time for the development of a second malignant growth. Hanlon in 1931 ascertained that 3 carcinomas occurred in an age group that averaged 63.6 years; that 2 cancers existed in a younger age (58.8 years) as compared with the average age (58.4 years) for single carcinomas. Warren and Gates in an excellent critical survey and statistical study of the literature to 1932 collected 1,259 cases and concluded that both multiple and single malignant tumors occur at about the same age and that any statement that the former occur at a more advanced age is contrary to the facts.

CRITERIA

Billroth, in 1869 reported the first case of multiple carcinomas and offered certain criteria which he felt had to be satisfied before the authenticity of a multiple cancer could be established. The postulates are that each tumor must differ histopathologically; must arise in a different location; each must be responsible for its own metastases. These criteria, while applicable to multiple malignant growths in different organs, cannot apply to those arising in the large intestine. It would

TABLE II.—AVERAGE AGE IN MULTIPLE CARCINOMA OF THE LARGE INTESTINE

	T	More than one
Collected cases (Warren and Gates)		
Collected cases (1933-1943)	66	6
Jewish Hospital series (1934-1943)	3	3
Total	79	30

Average age 54.8 yrs 59.9 yrs

be difficult to demonstrate histopathological differences considering that the tumors arise from similar epithelial cells. Nor can the third postulate be followed for reasons related to the above. Moreover, with early diagnosis and treatment, metastases are frequently absent. Therefore, the more liberal criteria suggested by Warren and Gates have been adopted for this study. They are that each tumor must be malignant, distinct, and one lesion cannot arise as a metastasis from the other.

CASE STUDY FROM THE JEWISH HOSPITAL (1934-1943)

This investigation is based on all carcinomas of the colon and rectum as encountered at this hospital during the 10 years (1934 to 1943). All are of proved malignancy; the tissue having been obtained by biopsy, laparotomy or autopsy. In this period there were 344 patients with cancer of the large intestine. Of these, 16 (4.6%) had multiple malignant growths. This incidence is about the same as that reported by many authors for multiple carcinomas in different organs. In three thousand surgical cancer cases, Owen found the frequency to be 4.7 per cent. Ward reported an even higher incidence, 5.2 per cent, in a series of 1,773 cases of skin cancer. In a collected series of 29,740 patients with carcinoma, Warren and Gates found the incidence to be 1.84 per cent. The few reported series of multiple malignant growths limited to the large intestine reveal a much lower incidence than we experienced. Thus, Brindley had 8 patients in a total of 306 cases (2.6 per cent). Abell encountered 1 in 131 patients (0.7 per cent) and Behrend found only 1 (0.6 per cent) in 158 cases of cancer of the colon and rectum.

Sex incidence and cancer site. Multiple carcinomas occurred more than twice as often in men as in women. There were 11 cases in the male as compared with 5 in the female sex. This ratio may in part be due to the fact that cancer in the large bowel is more frequently met in men. Railford, Heydemann and others have reported a 2:1 preponderance in single cancer in the male sex. The experience at our hospital does not corroborate these findings. In 344 patients there were 185 men with cancer in the large intestine as compared

TABLE III—DOUBLE CARCINOMAS OF THE LARGE INTESTINE—COLLECTED FROM THE LITERATURE (1933-1943)

Author	Reported	Sex	Age	Location	Location
Abell	953	M	40	Cecum	Transverse
Wick	913	M	37	Hepatic flexure	Sigmoid
Calkins	934	F	66	Pelvic colon	Descending colon
		F	68	Pelvic colon	Transverse
		M	60	Pelvic colon	Transverse
Pfeiffer	11	M	—	Descending colon	Rectosigmoid
		—	—	Rectum	Sigmoid
		—	—	Rectum	Sigmoid
Wenthall	915	—	—	Colon	Colon
Leinsohn	919	—	—	Colon	Colon
Thompson	916	M	5	Pelvic colon	Pelvic colon
		M	54	Cecum	Transverse
		M	56	Transverse	Ascending colon
Hark	946	M	50	Rectum	Hepatic flexure
Green	95	M	5	Rectum	Rectum
Freund and Sawyer	917	F	30	Hepatic flexure	Transverse
Behrend	937	—	—	Ascending colon	Rectosigmoid
Seibert	937	F	35	Rectum	Sigmoid
		F	64	Pelvic colon	Transverse
Hartokamen	937	F	—	Cecum	Transverse
Hawley	915	M	59	Splenic flexure	Ascending colon
		M	—	Rectum	Transverse
		F	5	Rectum	Transverse
		M	7	Sigmoid	Sigmoid
		F	6	Descending colon	Rectum
		M	5	Rectum	Rectum
		M	5	Rectum	Rectum
		M	—	Rectum	Rectum
		M	—	Pelvic colon	Rectum
		M	73	Pelvic colon	Rectum
		M	—	Transverse	Rectum
		M	—	Transverse	Rectum
Smith	—	—	—	Rectosigmoid	Rectum
	—	—	—	Rectum	Rectum
Law	—	M	—	Rectum	Rectum
	—	M	—	Rectum	Rectum
	—	M	—	Rectum	Rectum
Law	—	F	—	Rectum	Rectum

TABLE III—DOUBLE CARCINOMAS OF THE LARGE INTESTINE—COLLECTED FROM THE LITERATURE (1933-1943)—Continued

Author	Reported	Sex	Age	Location	Location
Schwartz and Harter	—	M	35	Sigmoid	Rectum
	—	M	44	Descending colon	Descending colon
	—	M	5	Rectum	Rectum
	—	F	5	Rectum	Rectum
	—	M	5	Descending colon	Rectum
	—	M	—	Rectum	Rectum
	—	M	7	Descending colon	Rectum
	—	M	—	Rectum	Rectum
	—	F	—	Sigmoid	Rectum
	—	F	—	Cecum	Ascending colon
	—	F	—	Ascending colon	Sigmoid
	—	F	—	Transverse	Cecum
	—	F	50	Rectosigmoid	Transverse
	—	F	—	Rectum	Sigmoid
	—	M	—	Sigmoid	Rectum
	—	M	75	Cecum	Sigmoid
	—	M	5	Cecum	Rectum
	—	M	—	Ascending colon	Rectum
	—	M	—	Descending colon	Cecum
	—	F	—	Rectum	Cecum
Wick	116 m	M	—	Transverse	Transverse
De Vries	9	F	—	Rectum	Sigmoid
Till	—	M	—	Rectum	Transverse
	—	M	—	Rectum	Rectum
Hersch and Menckner	—	M	7	Ascending colon	Sigmoid
Hefner	—	—	—	Pelvic colon	Descending colon
	—	—	—	Cecum	Cecum

11. Youngest patient
11. Oldest patient

with 159 in women a ratio of about 5:4 (Table I)

Age incidence. The youngest patient was 5 and the oldest, 71 years. One of the 14 cases with three carcinomas was 36 years of age. Eight were over 65 years, and 14 of the patient over 50 years (Table V). The average age for cancer occurring at a multiple lesion is 54 years.



Fig. Case 7. Metachronous carcinoma. The large intestine. Above splenic flexure, below rectum.

tients was found to be 56.1 years. Multiple carcinomas in the large intestine occurred at an earlier age. Thus in the combined series (Table II) the average age for 2 malignant growths was 54.8 years and for 3 or more cancers 51.9 years.

Multiple cancers and polyps. Lockhart Mummery, Warren, and Dukes have long emphasized the importance of considering polyps in the intestine as precancerous. Once a malignant change has occurred in a previously benign adenoma, difficulty may arise in identifying the cancer as having arisen in a simple polyp. These investigators have shown conclusively that such a change does occur more frequently than we suspect. The relationship

between multiple carcinomas and the presence of polyps led to an investigation of 84 consecutive necropsies on patients known to have died as a result of cancer of the large intestine. In 21 (25 per cent) one or more polyps were present. These were more frequent in colon carcinoma than in rectal malignant lesions. In patients with cancer in the rectum only 1 of 20 (5 per cent) had an accompanying polyp. Of the 16 cases with multiple cancers in the colon and rectum 6 (37.5 per cent) had polyps in addition to the malignant lesion. In 4 of these the polyp proved to be cancerous on microscopy. One patient (Case 10) was known to have had a benign polyp in the rectum at a time a splenic flexure cancer was removed. One year later he returned with an extensive infiltrating carcinoma in the place of the previously benign growth.

CASE REPORTS

CASE 1. M.S., a 45-year-old white female, was first admitted September, 1924, because of abdominal pain, constipation and loss of weight. Operation revealed a annular carcinoma of the transverse colon near the hepatic flexure. An exteriorization of the bowel was done followed by closure of the colostomy. She returned in 1934 with the same complaints. At exploration no evidence was present of a recurrence at the anastomosis, but the site was narrowed by scar tissue. In the belief that this pathology was the cause of her complaints the bowel was opened longitudinally

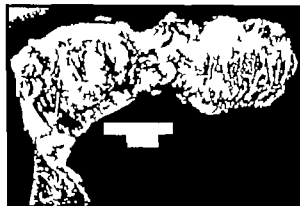


Fig. Case 3. Three synchronous carcinomas in the colon. a, left, present; one specimen, the trans-



verse colon T and i the splenic flexure. S b, right, photomicrograph of third carcinoma the descending colon.

ally and closed in the transverse axis. She reacted poorly from this procedure and died a few days later. At autopsy an unsuspected fungating carcinoma was found in the transverse colon near the splenic flexure.

CASE 2 M M a white male 50 years of age was admitted in June 1935 with epigastric pain nausea vomiting and anemia. He stated that 2 years previously he was operated upon for tumor but no resection was done. He then had a series of cancer serum injections followed by x ray therapy. On examination he presented a markedly cachectic and wasted appearance. There were 2 large masses in his abdomen one in the epigastrium and the other in the right iliac fossa. He died soon after admission. Necropsy revealed the presence of distinct cancers. The one was in the cecum and the second in the transverse colon had penetrated the stomach producing a ga. trocolic fistula.

CASE 3 C G a 28 year old white female was admitted in November 1935 with advanced intestinal obstruction and died 36 hours later. Autopsy uncovered both a constricting carcinoma of the sigmoid and an ulcerating malignant lesion 8 centimeters distal to the first lesion.

CASE 4 J L a 65 year old white man was admitted in June 1938 because of vomiting abdominal pain and weight loss. A cecostomy was done because of marked distention. Ten days later at operation 2 malignant lesions one in the splenic flexure and the other in the descending colon were noted. A Rankin obstructive resection was performed.

CASE 5 A G a 57 year old white male had a Rankin resection done in June 1939 for a carcinoma of the descending colon. Several months later he was admitted with intestinal obstruction. Operation showed a carcinoma of the transverse colon.

CASE 6 P L female white 51 years old was admitted in June 1939 with intestinal obstruction thought to be caused by adhesions secondary to a cholecystectomy (1924). Exploratory operation revealed an annular carcinoma of the transverse colon.



Fig 4 Case 16 Tx synchronous carcinomas S splenic flexure R rectum

Following a cecostomy he developed pneumonia and resection had to be delayed. After 7 weeks the lesion was removed and a primary anastomosis was done. Four months later a follow up investigation by means of a barium enema revealed a filling defect in the descending colon. Laparotomy confirmed the diagnosis of carcinoma.

CASE 7 D B a 62 year old white male was seen in January 1939 with intestinal obstruction. Re-



Fig 3 Case 15 Three synchronous carcinoma of colon and rectum. left (C) cancer T C in cecum and a second



at T a the transverse colon b right phten roentgenograph of a thick carcinoma occurring in the rectum

finding in patients not considered to have familial polyposis. The large intestine is a common site for the formation of polyps which according to Lawrence occur 12 times as frequently in the large as in the small intestine. Undoubtedly many carcinomas in the large bowel arise from pre-existing adenomas but there is no evidence to support the belief that all malignant growths in this area arise from this source.

Mayo found that polyps were present in 34 per cent of patients with cancer and that 14 per cent of these were already malignant. In contrast to this he found that in noncancerous patients polyps were found in only 16 per cent and 8 per cent of these had undergone malignant change. According to Hardy 40 per cent of all carcinomas of the large intestine start as benign polyps.

Our findings are almost similar and show a marked tendency to cancerous change in intestinal polyps in known cancer patients. Six of our multiple carcinoma cases (37.5 per cent) had polyps and in 67 per cent of these malignant transformation had occurred. How many of the remaining patients had cancer that arose in previously benign polyps could not be determined because the lesions were too extensive at the time the lesions were examined. It is conceivable that if cancer of the large intestine can arise in one area the tendency or susceptibility toward cancer can influence a similar transformation in a simple polyp. We cannot agree that all cancers in this region originate in previously benign polyps in view of our finding that polyps were present in only 25 per cent of our cancer cases and in only 5 per cent of rectal carcinomas. However the chances for a benign polyp to undergo malignant change in a patient known to have cancer in some other part of the large intestine or who belongs to a cancer family is great. These polyps should be attacked early and vigorously and not be allowed to grow. Our experience does not corroborate the statement by Boyd that once malignancy occurs in one of these adenomata the others tend to disappear.

Clinically and experimentally the evidence has accumulated against the belief that one cancer can bestow on the patient any degree of immunity against the appearance of a

second or even third cancer. Generally accepted now is the belief that malignant growths result from the action of an extrinsic force capable of causing abnormal cell growth on a susceptible intrinsic factor. Once a cancerous tumor has been removed from a patient, that individual should be suspect to the end of his days. He should be observed for evidences of other primary malignant neoplasms in the colon and rectum. Any polyp even if symptomless, should be removed early and not when the patient has a change in bowel habit, rectal bleeding and other evidences of malignant change. Whatever the susceptibility factor may be it is evident that the carcinogenic tendency is sufficiently strong to produce multiple cancers in certain people as easily as it produces single lesions in others.

Longevity in multiple cancers. The conclusion drawn by Hanlon and by Orr that patients with multiple cancers are older than those with single lesions is not confirmed by this study of multiple carcinomas limited to the large intestine. Hanlon claimed that because of earlier diagnosis and treatment, the survival period permitted the development of a second cancer. This in part may be true in malignant lesions occurring at different time intervals, but does not satisfactorily explain multiple cancers occurring synchronously. Warren and Gates basing their study on a large series of cases including those reported by Hanlon found the age to be no different for single than for multiple carcinomas.

Double lesions in the large intestine as we found them in the collected series combined with our own occurred 1.3 years earlier than our single cancers. Patients with three malignant neoplasms were 4.2 years younger than those with only one tumor. These findings contradict the belief that multiple carcinomas develop only on the basis of longevity.

Multiple cancers versus metastases. Skepticism might be entertained that multiple lesions are not primary new growths, but that one is a metastasis from the other. The problem of proving multiple primary cancers as they occur in the large intestine based on histopathology may at times be difficult in view of the fact that they arise from similar epithelial cells. When there is a difference in the histology

there can be no doubt of the authenticity of the case. But when the microscopic appearance is the same such genuineness cannot be easily established. The possibilities of fragments of cancer tissue breaking off the primary growth and becoming implanted on the mucous membrane at some other site must indeed be small. The passage of feces and mucus propelled by the constant peristaltic action would strongly influence the chances of any malignant cells clinging to the mucosa long enough to become a transplant. Certainly the chances are even less in those cases in which the older lesion is in the distal part of the bowel and the younger tumor tissue is more proximally located. One cannot claim metastatic origin of a double cancer if after removal of a second growth the patient should remain well and free from any evidences of the existence of metastases. Case 14 of our series offered incontrovertible testimony that similarity of the histopathology may occur and the multiple cancers can be primary tumors. Her three carcinomas were colloid adenocarcinoma indistinguishable from each other. Located in the sigmoid in the hepatic flexure and in the rectum successively removed in 1941, 1942 and 1944, no evidence at the time of the last operation was found of any metastatic spread. Final proof of the absence of metastases was offered at necropsy.

SUMMARY

1. The presence of a carcinoma does not confer immunity against the appearance of other primary cancers in the large intestine.

A predisposition or susceptibility to cancer is more important in the production of multiple carcinomas than chance, age or sex.

3. Sixty six cases of double and 6 patients with 3 cancers were collected from the literature since 1932. To these are added 13 patients with 2 cancers and 3 patients with three malignant growths.

4. Polyps were present in 5 per cent of single cancer patients and in 3, 5 per cent of those with multiple carcinomas. In 67 per cent of the latter group malignant degeneration had taken place.

5. The frequency of multiple cancers in our series was found to be 4.6 per cent.

6. There were 11 cases in men and 5 in women.

CONCLUSION

Multiple cancers can occur in the large intestine either synchronously or metachronously and the importance of keeping this in mind is apparent. The prognosis in cancer resections is influenced by the presence of a second malignant lesion in that if overlooked death of the patient may ensue because of the continued growth of the lesion.

Any patient who has had one carcinoma removed should be observed carefully and repeatedly for the possible development of a second new-growth. The use of the proctoscope, sigmoidoscope and contrast barium enema should be resorted to in every examination of the colon and rectum. The presence of a rectal carcinoma should be a signal to continue the investigation of the colon. The discovery of a colon lesion by roentgen ray or by palpation should be followed in every case by direct visualization of the lower intestine. Finally at operation a careful exploration of the entire bowel should be made. Unquestionably many poor results in the treatment of cancer of the large intestine can be attributed to the fact that a second lesion was missed. Brindley very aptly stated a patient with one cancer is a good subject for the development of a second and is more susceptible than one who is cancer free.

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FURTHER STUDIES ON THE PREPARATION AND USE OF SULFATHIAZOLE OINTMENT IN THE TREATMENT OF BURNS

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THE use of sulfathiazole ointment in the treatment of burns has been previously reported by Allen, Owens, Evans and Dragstedt (4). The purpose of this report is to describe further observations on the preparation and use of several kinds of sulfathiazole ointment and to present an evaluation of these from the standpoint of emulsification properties, stability, effect on the healing of tissues, sulfathiazole diffusion, and bacteriostatic properties.

The general recent trend in local burn therapy has been to utilize some sort of grease dressing in view of the accumulating evidence that the tannic acid treatment of burns has a number of undesirable features such as contributing to liver necrosis (26) and delaying epithelial regeneration (8).

An ordinary petrolatum or vaseline dressing is probably the most widely used local treatment for burns at the present time due in large measure to the excellent results reported by Allen and Koch (3) and by Siler and Reid (21). For burns which can be cleansed and treated soon after the burn occurs the petrolatum dressing appears to be quite a satisfactory method, especially when fine mesh gauze and pressure dressings of mechanics waste are used. However, if the burned area has an opportunity to become contaminated and considerable delay is encountered before final treatment is instituted, it is possible for severe infection to develop. This may not only delay healing but may also destroy viable nests of epithelium in the burned area which would

otherwise offer a nucleus for regeneration of an epithelial surface. It is especially for such cases in which cleansing procedures are not feasible and in which contamination or beginning infection has occurred that there is a place for a bacterial inhibiting agent in what ever grease dressing is utilized for local therapy. It is possible to obtain an effective inhibition of bacterial growth in burned areas by the use of sulfonamides administered systemically as was reported in the symposium on the management of the Coconut Grove burns at the Massachusetts General Hospital by Cope, Lyons, Cannon. However, this requires the maintenance of a therapeutic blood level which presents certain hazards and problems in the care of many severely burned patients, especially when adequate laboratory facilities are not available.

To obtain appreciable diffusion of sulfathiazole from a petrolatum base, it is necessary to add some type of surface active agents to the ointment base. This surface active agent may permit the emulsification of petrolatum with water, thereby permitting the sulfathiazole to be liberated from the aqueous phase of the emulsion. Or as we have found, the surface active agent may permit the liberation of sulfathiazole from the petrolatum without emulsification. There are a great many surface active agents which are recently available (25) and their special properties lend themselves to uses in many ways not only in therapeutics but also in various commercial industries such as in cosmetics, paints, insecticides, and so forth. The emulsification and sulfathiazole diffusion properties of such proprietary ointment bases as Aquaphor or Hydrosorb which are for the most part composed of petrolatum are due to the presence of certain surface ac-

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This work was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago.
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tive agents added to the petrolatum. These proprietary bases have been studied and in addition ointments have been made up with petrolatum to which varying concentrations of known surface active agents were added.

The surface active agents which have been studied particularly have been the Atlas spans and tweens (5). This represents a group of mannitol and sorbitol derivatives (22) which vary in their physical properties from thin liquids to viscous oils or waxes. These materials which are nonelectrolytes, vary from complete oil solubility to complete water solubility. The spans are predominantly oil soluble and water insoluble, although they are dispersible in water. The tweens are for the most part soluble in water. Each of these surface active agents have properties which lend themselves to particular uses. Of these agents the most satisfactory for obtaining a stable petrolatum water emulsion was found to be arlacel C which is a purified form of span 80 and is essentially sorbitan monooleate.

The spans and tweens are miscible with each other and in some instances may be combined to obtain a particular surface action phenomenon not possessed by either separately. For example it was found that when tween 80 was added to the aqueous phase of a petrolatum water emulsion, the diffusion of sulfathiazole from such an emulsion was appreciably greater than when only arlacel C was used for producing the emulsion. Furthermore it expedites the liberation of sulfathiazole from petrolatum even when the petrolatum has not been emulsified with water. Tween 80 which is a polyoxyalkylene ether of a partial oleic acid ester was also found to increase slightly the solubility of sulfathiazole in aqueous solution and to increase the extent to which sulfathiazole powder could be suspended in water. Another feature of the tween 80 was its detergent properties which are applicable in the cleansing of wounds contaminated by oils or greases where one would not choose to use an irritant solvent.

Two general classes of sulfathiazole ointments were studied. The nonemulsion ointments were prepared by adding sulfathiazole to a proprietary petrolatum base such as

hydrosorb or aquaphor or to petrolatum which contained spans or tweens or both. The emulsion ointments were prepared by adding sulfathiazole in water to these grease bases. The method of preparing the ointments is complicated by the fact that heat sterilization of these materials after mixing results in the sulfathiazole caking or settling out in the grease base or separation of the emulsion. In view of the bacterial contaminations found in sulfonamide ointments by Fisher the ointments which were designed for clinical use were prepared in the operating room from ingredients which had been subjected to heat sterilization and then mixed under sterile precautions, with the aid of a manual or electric mixer.

A laboratory test was devised for evaluating the diffusion of the sulfathiazole from the various ointment preparations. This was carried out by suspending 10 grams of ointment in a fine mesh gauze bag in a jar containing 100 cubic centimeters of water. The determinations of the sulfathiazole content of the water were made after varying periods, changing the water from time to time to ascertain the extent to which the diffusion was maintained. The results of this are presented in Table I.

These observations demonstrate that certain surface active agents expedite the diffusion of sulfathiazole from a petrolatum base into a surrounding aqueous medium. In the nonemulsion ointment series, there were some instances in which proprietary bases did not liberate sulfathiazole much better than petrolatum alone. In other instances there was an appreciable liberation of sulfathiazole which was most marked in the first 24 hours, although subsequent liberation was somewhat reduced. The concentration of sulfathiazole in the ointment base did not appear to make much difference in the rate and amount of sulfathiazole diffusion in most instances. The emulsion ointment preparations demonstrated better original diffusion and continued diffusion than the nonemulsion ointments. The ointment which appeared to have the most satisfactory stability and diffusion properties was the one prepared from petrolatum with arlacel C in the oil phase and tween 80 in the aqueous phase with sulfathiazole (Formula).

FORMULA

Oil phase	
Petrolatum	48 c.c.
Arlacel C	2 c.c.
Aqueous phase	
Sulfathiazole	5 gm.
Tween 80	$\frac{1}{4}$ c.c.
Water q.s. d	100 c.c.

One of the methods of evaluating the various ointment preparations was to apply these to the raw surface of a dermatone graft donor area and observe the effect on healing such as was described by Cannon and Cope (8). These tests showed that the sulfathiazole ointments did not appreciably retard healing as compared with petrolatum. In a few instances there was some delay in epithelization as compared with petrolatum although in many instances the sulfathiazole ointment appeared to contribute to a more rapid rate of healing than was observed for petrolatum. Tannic acid was found to delay epithelization when compared with petrolatum as was pointed out by Cannon and Cope. Evidence of maceration of the tissues was less frequently observed with the emulsion type of ointment than with the nonemulsion ointments.

In regard to the observations made subsequent to healing it was found that a considerable proportion of the donor areas treated with sulfathiazole in aquaphor developed keloids. This was also observed with other sulfathiazole preparations from time to time. However there was distinctly less tendency for the emulsion ointments to be associated with keloid formation than the nonemulsion type. Tannic acid did not lead to keloid formation in any of the donor areas in our series. Petrolatum was seldom associated with keloid formation. Sulfathiazole crystals applied to donor areas which were then covered with petrolatum did not appear to be associated with keloid formation except in one instance. The emulsion ointments containing arlacel C and tween 80 appeared to be associated with keloid formation less frequently than the emulsion ointments prepared from proprietary absorption bases.

One instance of sensitivity to sulfathiazole was observed when 1 gram of sulfathiazole crystals was applied to part of a dermatone donor area. This patient had been given sul-

fathiazole by mouth about 8 months previously and he had developed evidence of sensitivity at that time. The donor area exhibited a marked local sensitivity reaction consisting of itching and burning and a continual bleeding from this area which lasted several days even though the sulfathiazole was removed in the first 24 hours. There was definite delay in epithelization in this area as compared with the area which was covered originally with petrolatum alone. In addition the patient exhibited a generalized sensitivity reaction consisting of itching urticaria and erythema.

Sulfathiazole ointment has been used in the treatment of 60 cases of burns at the University of Chicago Clinics. The ointment preparations which were used consisted of 5 per cent or 20 per cent sulfathiazole in aquaphor, 5 per cent sulfathiazole in aquaphor water emulsion and 5 per cent sulfathiazole in petrolatum water emulsion (water in oil type of emulsion with arlacel C and tween 80 as surface active agents).

The preliminary treatment which was carried out with rigid aseptic precautions consisted of gentle cleansing of the burned surface with soap and water and copious irrigations with physiological saline solution. Débridement of easily detachable skin was done and usually the blisters were opened. Adequate sedation was obtained with morphine and it was not found necessary to use general anesthesia on any of these cases. Cultures of the burned area were usually taken before and after the cleansing procedure. Photographs were taken in most of the cases before the treatment was started.

The ointment was spread on fine mesh gauze (40 by 44) and applied to the burned area. Large amounts of mechanics waste were spread over the gauze and wrapped securely with bandages to obtain the desired pressure effect on the burned area. Additional compression was obtained in some cases by the use of elastic bandages on the extremities or elastoplast adhesive on the trunk. A rather important point which has been consistently observed was the analgesic effect of the sulfathiazole ointment. This has made it possible to minimize sedation to a considerable extent as this analgesic action is usually noticed im-

TABLE I.—DIFFUSION OF SULFATHIAZOLE FROM 10 GRAMS OF OINTMENT INTO 100 C.C. OF WATER AT 57° C. IN MILLIGRAMS

	0- Day ¹	Day ₁	2 Days ¹	3-5 Days ¹	5-15 Days
Petrolatum base (without water)					
Petrolatum with 5 per cent sulfathiazole	0	Trace	7	Trace	Trace
Amerchol with 5 per cent sulfathiazole		Trace	2	2	
Aquaphor with 5 per cent sulfathiazole	2	7		2	
Aquaphor with 20 per cent sulfathiazole	2	Trace		Trace	77
Hydrosorb with 5 per cent sulfathiazole	7	Trace	5	Trace	25
Petrolatum with 5 per cent sulfathiazole, 10 per cent Tween 80	22	2		Trace	Trace
Petrolatum with 5 per cent sulfathiazole, 15 per cent Tween 80	12		2	Trace	
Petrolatum-lanolin 5 per cent sulfathiazole		Trace	2	Trace	Trace
Petrolatum-lanolin 20 per cent sulfathiazole	5		14		
Petrolatum-water emulsion (50 per cent water)					
Amerchol with 5 per cent sulfathiazole	7	2	2		5
Aquaphor with 5 per cent sulfathiazole	5		7	5	54
Hydrosorb with 5 per cent sulfathiazole	5		52		5
Petrolatum with 10 per cent alcohol C & 5 per cent sulfathiazole, 15 per cent Tween 80	20	5	10	5	125

¹Indicates change of water to determine continued diffusion of the sulfathiazole from the ointment

mediately after the application of the ointment.

Blood counts and cell volume determinations were made in the more severe burn cases and plasma was administered as needed. It was of interest to note that in one patient who was treated within 20 minutes after the burn occurred there was a hemocentrifugation of 12 per cent during the course of the cleansing and dressing procedure which required about 30 minutes. This point will be discussed in relation to the effectiveness of the pressure dressings in preventing loss of plasma.

The original dressing applied to the burned area was generally left in place for 10 days to 2 weeks. When the dressing was removed at this length of time many of the burned areas were completely healed. If the healing was not complete the sulfathiazole ointment was reapplied and left on for another week. In this series of cases there was only one which was not substantially healed in 3 weeks and which required skin grafts. This does not include the original cases reported by Allen and associates in which it was necessary to resort to skin grafts in 2 cases.

In the cases in which the emulsion type of ointment was used it was of interest to note that in many instances the skin surface was dry and free from evidence of maceration at

the time of the removal of the dressing. Dry scaly crusts were often adherent to the skin or to the dressing. When there were raw surfaces present there was very little exudate on the dressing in many of the cases. Cultures were usually taken after the removal of the dressings and photographs made.

In regard to the one case in this series which required skin grafts the original dressings were removed on the eighth day at which time the burned skin of the leg appeared to be viable throughout and there was no evidence of infection. The leg was then treated with frequent changes of so called sterile saline dressings throughout that day and then fresh sulfathiazole ointment was reapplied that evening. When the dressings were changed again 1 week later there was obvious infection and necrosis of a considerable portion of the burned skin. It is probable that the infection was introduced during the course of the saline dressings. The bacteriostatic properties of the ointment were apparently not adequate to control the infection in this instance. The ointment used was the nonemulsion aquaphor preparation which was subsequently found to liberate less sulfathiazole than the emulsion type of sulfathiazole ointment.

The cultures taken before the cleansing procedure frequently demonstrated Staphylo-



Fig. 1. H. K., aged 21 years, burned right forearm by boiling water 3 days previously and originally treated by batesin pectate. Cultures of blister fluid showed *Streptococcus viridans* and *Staphylococcus albus*. a left Condition of forearm at time of admission. Cleansing with soap and water and débridement followed by irrigation was carried out (without general anesthesia). The raw surface was covered with 5 per cent sulfathiazole emulsion ointment (aquaphor 15 per cent, water 80 per cent) on fine mesh gauze. A pressure dressing was then applied. The dressing was left on for 12 days and then removed when there was

no evidence of healing except for few small raw surfaces. There was no evidence of exudate on the dressings and the skin was free from any evidence of maceration. Ointment was reapplied until 3 weeks after the burn when all raw surfaces were healed over. The blood sulfathiazole determinations showed only a trace of sulfathiazole but the determinations on the urine showed 0.5 gram in the first 24 hours and from 1 to 10 milligram for the following week. b right Condition of forearm 29 days after the burn when healing has been complete for over a week. There are a few red areas but no evidence of residual keloid or contracture.

coccus aureus of the hemolytic type. In a number of cases *Streptococcus hemolyticus* was recovered from the burned area and in 1 case *Streptococcus viridans*. *Staphylococcus albus* was also a frequent contaminant. The cultures taken after the cleansing procedure were often sterile but organisms found prior to cleansing were not infrequently present but less abundant in amount. Cultures taken after the original dressing was removed at 10 to 14 days were either sterile or demonstrated the presence of some of the organisms originally present. Some positive cultures were obtained after complete healing had occurred and obviously were not of practical significance.

In general it can be said that these burn cases represented what can be considered second degree burns judging from the excellent results which were usually obtained except for the one case which developed infection. However if a bacteriostatic agent had not been used on the burn cases which came in a day or more after the burn with positive cultures of pyogenic organisms it is probable that infection would have developed in the burned skin in some instances. This would have destroyed the remaining viable epithelial elements and thus prevented spontaneous regeneration of an epithelial surface. These cases then would have been classified as third degree burns on the basis of the end results.

A most interesting feature of this work on sulfathiazole ointments has been the use of surface active agents to obtain liberation of a water soluble medication from a petrolatum base. There are many instances in which it is desirable to have a grease base as a vehicle for a water soluble medicament but unless some type of surface active agent is utilized the medication may remain imprisoned and relatively inactive. Lanolin has some surface active properties and has been widely used as a vehicle for water soluble medications.

Proprietary absorption bases utilize the principle of incorporating surface active agents such as diethanolamine oleate or cholesterol esters of oleic acid in petrolatum. These commercial absorption bases are designed for a wide field of usefulness in the pharmaceutical and cosmetic trade and may not necessarily represent the most desirable concentration or selection of surface active agents for particular needs. In view of the results obtained with the sulfathiazole diffusion tests on absorption bases it would appear that improvements could be obtained in commercial bases designed primarily as vehicles for water soluble medications. The surface active agents which are most appropriate from the standpoint of obtaining good emollient properties in an ointment are not necessarily the most efficient for obtaining liberation of water soluble medications from petrolatum.

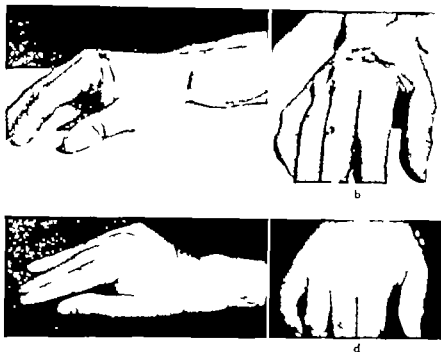


Fig. 1. J. G. aged 5 yrs., received burn of hand and wrist from benzene flame 20 minutes prior to admission. a, Condition of hand and wrist at time of admission immediately after burn. Cultures demonstrated *Staphylococcus albus*. b, Same. The hand and wrist were cleansed with soap and water. Débridement of separated skin as carried out. Irrigation with physiological saline solution, and application of 5 per cent sulfathiazole emulsion ointment (AquaPhor 5 per cent Ster 80 per cent) on fine mesh gauze as carried out. Then pressure dressings of mechanical cast were put on. The dressings are left on for 3 days, at which time the hand was healed except for few flaky crusts. Ointment dressing reapplied, and removed following 1 week, at which time hand was completely healed. c, Condition of hand at end of 7 weeks. There was no evidence of residual scarring or contracture. d, Same as c.

The fundamental mechanism of the action of these surface active agents appears to be primarily a matter of altering the opposing surface forces at the oil and water interface. These agents are mixed polar nonpolar molecules which presumably exist as thin films oriented at the surface or interface with their hydrophilic heads toward the aqueous phase and their hydrophobic chains away from it. By proper balancing of the hydrophobic hydrocarbon chain with hydrophilic groups the desired clearance or diffusion of the water soluble medication is obtained from the petrolatum base or the petrolatum water emulsion.

In regard to the data on the cultures it was found that organisms could often be cultured from the burned area after the cleansing débridement and irrigation procedure. In most instances, however, the number of colonies

which grew out was appreciably less as compared with cultures taken before the cleansing procedure. The evidence from the culture studies favors the view that these preliminary cleansing procedures are helpful in minimizing the magnitude of bacterial contamination in burned areas but not effective in completely eliminating it. There can be little doubt that cleansing débridement and irrigation have a place in the handling of burns as well as in other wounds wherever it is feasible to carry out such. It would be an unfortunate choice to omit these rather fundamental procedures in the treatment of wounds unless the facilities were not available to do so.

The demonstration of bacterial contamination in a burned area after relatively thorough cleansing débridement and irrigation lends support to the view that the local burn dressing should contain some bacteriostatic agent



Fig. 3. K. S. aged 18 months, suffered burn of face and elbow from hot grease one day previously at which time a tannic acid jelly was applied to face. a, Condition of face and elbow at time of admission. Cultures demonstrated abundant growth of *Streptococcus hemolyticus* and *Staphylococcus aureus hemolyticus*. Very gentle cleansing was done with soap and water followed by irrigation with physiological saline solution and then application of 5 per cent

sulfathiazole emulsion ointment (aquaphor 15 per cent, water 85 per cent). Physiological saline dressings applied alternately for first 3 days to hasten removal of tanned crusts. b Face 3 days after burn. Healing has occurred except for small crusted areas which healed over within the next 5 days. c Condition of face 48 days after burn. There is no residual redness or scar visible at this time.

to deal with any residual contamination. If no cleansing procedures are used there is even greater need for a bacteriostatic agent. In cases in which considerable delay has occurred before the burn has had treatment and some degree of infection has already developed there is again even more urgent need for some agent which could minimize or prevent further development of infection in the burned area. Petrolatum does not possess any inherent bacteriostatic properties. Its main virtue is that it is relatively inert and permits healing to progress under its protective cover unless the residual epithelial elements have been destroyed by the burn or by the development of infection.

To meet the need for a bacteriostatic agent in the local treatment of burns, the use of sulfathiazole in a petrolatum base which permits the diffusion of the sulfathiazole offers a reasonable means of minimizing or controlling the development of infection in the burned area. In view of the excellent results which were obtained with petrolatum alone by Allen and Koch and Siler and Reid it would appear desirable to continue to utilize petrolatum as the principal protective covering material on burned areas. The desired diffusion of sulfathiazole from the petrolatum can then be obtained by the use of the appropriate surface active agents.

It is appreciated that there is as yet no general agreement regarding the value of the local application of chemotherapeutic agents in the prevention and treatment of wound infections (20). The efficacy of the sulfonamides in the treatment of many infections such as pneumonia and gonorrhea, however, may be regarded as definitely established. In these cases a factor in the success seems to be the production of a bacteriostatic concentration of the drug in the body fluids in contact with the invading parasite. In wounds the contaminating organisms are frequently sequestered or protected by their incorporation in coagulated protein exudates, necrotic tissue or foreign bodies. Many of these organisms are susceptible to the bacteriostatic action of the sulfonamides and these drugs have apparently very little effect on the growth of body cells. These facts present a challenge to the surgeon to control the various unfavorable factors in wounds so that he can secure for his patients the beneficial features of modern chemotherapy now enjoyed by his medical colleague. As emphasized by Whipple much can be accomplished in this direction by good surgery and for this there is no substitute. Of all types of wounds, it has appeared to us that burns present those features most favorable for the local use of chemotherapeutic agents. Foreign bodies are usually absent, surface

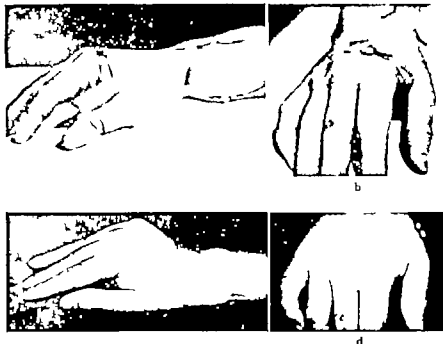


Fig. 1. G. aged 5 years, recent burn of hand and wrist from benzene flame 30 minutes prior to admission. Condition of hand and wrist at time of admission immediately after burn. Cultures demonstrated *Staphylococcus* *flexus*. b, Same. The hand and wrist were debrided with soap and water. Debridement of separated skin was carried out. Irrigation with physiological saline solution, and application of 5 per cent sulfathiazole emulsion or tincture (Aquaphor 5 per cent, tincture 80 per cent) on fine mesh gauze was carried out. Then pressure dressings of mechanical waste were put on. The dressings were left on for 3 days, at which time the hand was healed except for a few flaky crusts. Ointment dressing reapplied, and removed following week at which time hand was completely healed. c, Condition of hand at end of 7 weeks. There was no evidence of residual scarring or contracture. d, Same as c.

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Fig. 4. M. C. aged 45 years, suffered hot water burn day previously. Burn of back and elbow. Cultures demonstrated *Streptococcus hemolyticus* and *Staphylococcus aureus hemolyticus*. (Treated and debrided without general anesthesia and application of 5 per cent

sulfathiazole emulsion ointment (petrolatum 45 per cent, sulfathiazole 5 per cent, petrolatum 45 per cent, petrolatum 45 per cent). Back and elbow 4 days after burn. Approximately three fourths of burned area has healed. Condition of back 15 days after complete healing for several days.

contamination only exists at least in the early cases and adequate drainage is most easily obtained.

In regard to the matter of whether sulfathiazole in an ointment base has any penetrating properties when applied locally, the work of Strakosch and Clark (23, 24) has demonstrated that a tissue concentration of 4 to 8 milligrams per cent may be obtained in the skin from the application of a sulfathiazole ointment comparable to what was used on our burn cases. Furthermore in the extensive work of Ackman and Wilson of Gurd and their co-workers it was found that considerably higher tissue concentrations of sulfathiazole were obtained with their emulsion ointment when it was applied to raw surfaces which were not covered with skin. The results obtained by these two groups of workers establishes quite definitely that sulfathiazole can penetrate the tissues in sufficient concentrations to have a bacteriostatic effect when applied locally in an appropriate ointment vehicle.

Gurd and his co-workers have made several reports on the use of their sulfathiazole emulsion ointment in the treatment of burns. They have had very satisfactory results with this

ointment in controlling infection in burned patients. The original report by Ackman and Wilson of the use of this emulsion ointment in the treatment of burns as well as other conditions, appeared just prior to the article by Allen and associates (4) although the use of the sulfathiazole ointment was apparently inaugurated at about the same time. The extensive series of burns reported by Evans and Hoover which were treated by the application of a sulfanilamide ointment deserves mention as important additional evidence of the effectiveness of local sulfonamide therapy. With the use of their sulfanilamide ointment (6 per cent sulfanilamide in lanolin and cold cream) their problem of infections in burned patients has practically ceased to exist.

In reviewing the results of the burn cases in our series it was rather gratifying to find that spontaneous healing occurred except in one case which developed an infection and subsequently required skin grafting. This series included a number of patients who were seen from 1 to 5 days after the burn and had positive cultures of *Staphylococcus aureus hemolyticus* and in some instances *Streptococcus hemolyticus*. The extent to which healing progressed under these rather unfavorable

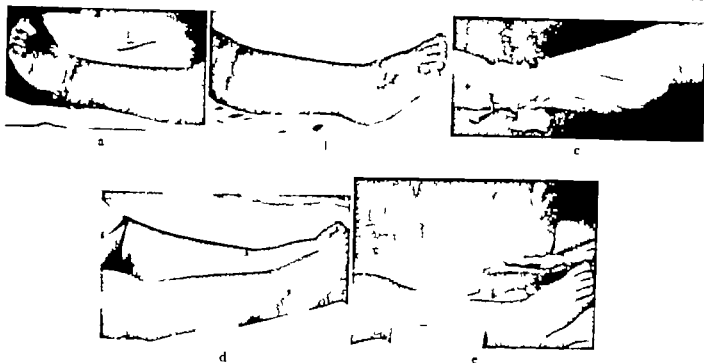


Fig. 5. B. B. aged 21 months, received a hot scald 5 days previously from bathtub accident. On admission the temperature was from 38.2 C. to 38.8 degrees C. the hematocrit was 36 per cent and the plasma protein 4.6 grams per cent. a, Extensive burn of left foot and leg from just below knee at time of admission. Gentle cleaning, debridement, and irrigation with physiological saline solution was done and 5 per cent sulfathiazole emulsion ointment (petrolatum 48 per cent, arlacel C 2 per cent, water 45 per cent, tween 80 3 per cent) was applied in fine mesh gauze. Pressure dressing with mechanics waite was then put on. b, Extensive burn of right foot and leg from just below knee with dressing already applied to left

leg. c, It res. f both legs demonstrated heavy growth of *Staphylococcus aureus* bet. olyticus. Both legs had appearance of second degree burn with probable areas of third degree burn. Blood transfusion of 160 cubic centimeters given. Back of left leg at time of admission with detached layer of epidermis. d, Condition of burned legs 2 weeks after treatment with emulsion ointment when original dressing was removed. There was little evidence of exudate on the dressing the burned area was dry and healed. There were a few dry scaly crusts. Highest blood sulfathiazole level was 0.4 milligram per cent. e, Excellent condition of both legs 3 weeks after treatment, with complete healing.

circumstances appeared to us to be good evidence that the sulfathiazole had minimized infection sufficiently to permit the remaining epithelial remnants in the burned area to regenerate an epithelial surface. This spontaneous regeneration does not occur in the presence of a manifest infection or at least is very considerably retarded.

In view of our experience with a bacteriostatic agent in the local burn dressing there would appear to be a place for some basic revision of the present classification of burns, to distinguish second degree burns which heal spontaneously from viable epithelial remnants in the burned area from second degree burns in which these viable epithelial elements become destroyed or damaged by infection. For practical purposes this latter group are now classified as third degree burns because healing occurs only with the aid of skin grafts or after long periods of peripheral epithelialization. It is

this group of cases which offers a promising field for the use of local bacteriostatic agents to prevent infection and the destruction of epithelial remnants in the burned area from which spontaneous regeneration of an epithelial surface may occur.

The problem of the use of sulfathiazole or any other sulfonamide revolves to some extent about the matter of developing sensitivity to these drugs. In view of the widespread use of sulfonamides one may expect an appreciable incidence of sensitivity. There have been recent reports of a relatively high incidence of sensitivity to sulfathiazole ointment (10). With an ever increasing number of people who have had some form of sulfonamide therapy the time may come when the problem of sensitivity may contraindicate the use of a sulfonamide ointment on the burned patient unless a preliminary test has been carried out to eliminate the possibility of sensitivity.

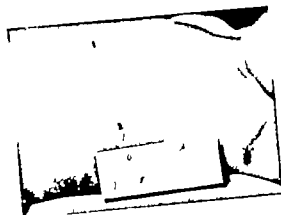
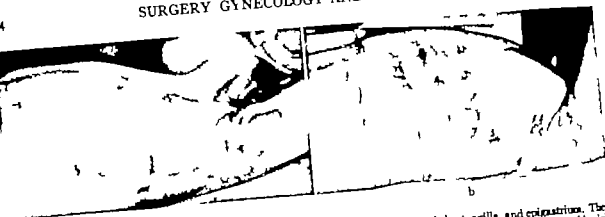


Fig. 6 J. K. aged years, received hot water burn days previously from bathtub accident. On admission temperature was from 38.7 C. to 39.8 degrees C. on first day hematocrit was 35 per cent, and the plasma proteins were 6 grams per cent. a, Extensive raw surface. b, Time of

admission over side of chest, axilla, and epigastrium. There were smaller areas on right side of chest and in right groin and on right side of buttock. Cultures from the raw surface demonstrated heavy growth of *Streptococcus hemolyticus* and *Staphylococcus aureus* hemolyticus. After the cleansing and irrigation with physiological saline, done without general anesthesia. Five per cent sulfathiazole emulsion ointment (petrolatum, 48 per cent, arched C per cent, tween 80 1/4 per cent, water 45 per cent) was applied on fine mesh gauze. Mechanics' wrist pressure dressing applied. Blood transfusion of 200 cubic centimeters was given. b, Condition of burned area. c, Six weeks later when first dressing was changed. There has been considerable healing of the burned area of the chest as well as other regions. General condition of patient quite good at this time although for the first 5 days after admission there was moderate febrile reaction. The blood sulfathiazole level reached 1 milligram per cent. c, Almost complete healing of burned area on chest present. d, End of 3 weeks. The few remaining crusted areas were healed within another week. This case demonstrates that spontaneous healing may occur if a bacteriostatic agent is used in the local treatment.

However for patients who are not sensitive to sulfathiazole the use of sulfathiazole ointment for a burned area has given such gratifying results in our experience that this form of treatment for burns deserves consideration. Furthermore in the extensive use of sulfathiazole emulsion ointment for burns and other wounds Gurd and co-workers have not had any serious difficulties from sensitivity nor have Evans and Hoover from their sulfanilamide ointment.

A rather important point in the use of sulfathiazole ointment for burns is that no high blood levels were encountered in this series of cases. The maximum blood level was not more than 2 to 3 milligrams per cent even in cases with extensive raw surfaces. Gurd and his co-workers also found relatively low blood levels of not more than 3 to 4 milligrams per cent, when they used a sulfathiazole emulsion ointment in the treatment of

burns or other wounds. This point is of considerable significance in the treatment of patients under conditions in which laboratory facilities are not adequate for determining sulfonamide blood levels. Evans and Hoover found blood levels of only 1 to 2 milligrams per cent when they used sulfanilamide ointment.

Furthermore in severe burn cases in which urinary secretion may be considerably diminished it would obviously be unwise to use sulfonamides locally unless the absorption rate could be controlled to some extent by a vehicle such as the ointment base described in this work which permits only a gradual liberation of sulfathiazole.

The systemic administration of sulfonamides in concentrations which are adequate to maintain a therapeutic blood level and an appreciable bacteriostatic effect in the burned area would also appear to have its disadvantages.

vantages in the severely burned patients when kidney function as well as liver function may be diminished. If one can obtain a desirable bacteriostatic effect by the local application of a sulfathiazole ointment without the danger of overwhelming systemic absorption it would seem unnecessary to subject a burned patient to the systemic administration of sulfonamides to obtain the desired local bacteriostatic effect, especially if there was appreciable impairment of renal and hepatic function.

With respect to the use of solvents such as benzene for removing heavy oil or grease from a burned surface attention should be drawn to the fact that benzene is a powerful tissue irritant and is capable of producing a chemical burn in normal intact skin. It is clearly undesirable to utilize such a solvent to remove grease from a thermal burn when in so doing some degree of chemical burn is superimposed. Tests are being conducted to determine the most desirable surface active agent which might be utilized in an aqueous solution for removing grease to replace the need for using a solvent which has tissue-damaging properties. Our observations thus far would lead us to believe that tween 80-5 per cent in physiological saline solution will serve this purpose to a considerable extent.

In regard to the effect of the pressure dressings advocated by Allen and Koch and which were used in most of the burn cases reported here it is probable that this has minimized to some appreciable extent the loss of plasma into the tissues or from the burned surface. It has not obviated however the need for plasma transfusions. In experimental and clinical observations on the rapidity of plasma loss after a burn it would appear that a substantial part of the plasma loss may occur within the first half hour and unless the pressure dressing is applied within this length of time this original substantial loss would not be controlled. However the control of subsequent loss would undoubtedly be favorably influenced by the pressure dressing. For the treatment of the plasma loss a chart has been devised by us (17) which is based on the hematocrit reading and the body weight. This has aided considerably in evaluating the plasma requirements of burn patients.

The pressure dressing undoubtedly influences the course of the burn patient from the standpoint of promoting the venous return from the dilated capillaries in the burned area. This point has not received the proper attention it deserves and even if some choose to discount entirely the effect of the pressure dressing in minimizing plasma loss there can be little doubt but what pressure is beneficial to the survival of skin which has been damaged by heat. In skin grafting it is frequently observed that venous stagnation may occur in the graft. If this is not controlled by pressure dressing a graft may slough off even if it has appeared to be a perfect take. This is especially true of skin grafts on the leg where the venous return is particularly poor when the leg is in a dependent position. If viable skin grafts can undergo necrosis from venous stagnation it is not at all improbable that burned skin which is on the borderline of viability may also undergo necrosis from venous stagnation which could otherwise be obviated by a pressure dressing. Aside from the favorable influence of the pressure dressing in aiding venous return the fundamental principle of utilizing the forces of gravity should not be overlooked in supplementing venous return by elevation of the burned part in so far as this is feasible.

For a complete discussion of the various aspects of burns reference should be made to the extensive work of Harkins.

SUMMARY

Sulfathiazole emulsion ointment (see formula page) was found to be very satisfactory in the treatment of burns and would appear to be especially suited to the first aid type of burn treatment when cleansing procedures may not be feasible because

1. There is sufficient liberation of sulfathiazole from the ointment to have at least some bacteriostatic effect which is not obtained by grease dressings alone.

2. The liberation of sulfathiazole is controlled in this ointment preparation to the extent that overwhelming systemic absorption of the sulfathiazole does not occur. It is therefore feasible to treat burn patients with this ointment under conditions where it may

not be possible to follow the blood sulfonamide level by laboratory tests.

3 The liberation of sulfathiazole from the emulsion ointment is continued for a period of a week or more and thus permits a continuous bacteriostatic effect.

4 The sulfathiazole emulsion ointment has an analgesic effect on the burned surface which minimizes the extent of sedation required and thus keeps the patient in a relatively more ambulatory condition.

5 The emulsion ointment can be removed from burned areas with less difficulty than can ordinary grease dressings if it should be desirable to change the dressings.

6 The emulsion type ointment may be easily prepared from sterile ingredients when it is needed with a simple salad dressing mixer.

CONCLUSIONS

The principle of the use of a bacteriostatic medicament in a bland grease base containing surface active agents which aid in the liberation of the bacteriostatic medicament offers a promising approach to the problem of the local treatment of burns, especially from the standpoint of controlling infection.

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ROENTGENOGRAPHIC INTERPRETATION OF WHAT CONSTITUTES ADEQUATE REDUCTION OF FEMORAL NECK FRACTURES

ROBERT T. McELVANY, M.D. Chicago, Illinois

THE worth of any opinion cannot be evaluated until the facts and the interpretation of those facts on which the opinion is based are presented for consideration. The statements to follow are the result of observations made over a 6-year period. These observations include studies made of roentgenograms taken from large bone and joint services of patients in private practice and of cases of friends and associates. The series of cases used to illustrate this paper are taken from the writer's private practice.

No particular technique or gadget for the internal fixation of an intracapsular fracture of the femur is advocated. The fixation must be adequate, correctly placed, and in direct line of weight thrust. In this author's experience the cannulated Smith Petersen nail has fulfilled the above functions better than have wires, screws, bolts, or multiple pins.

An excellent result in this type of fracture is one in which (a) there is no pain or spasm; (b) there is no limp; (c) there is equal leg length; (d) there is a complete range of active hip motion including full internal rotation; (e) the patient to walk and climb requires no external aid; (f) on roentgenographic examination the neck is of practically normal length, the head is smooth with normal density, the joint space is maintained, and the fracture has healed with unbroken lines of trabeculation crossing the fracture site.

No attempt is made to evaluate the rôle of blood supply as a cause of nonunion or the development of a dead head. This paper deals with only the immediate results, that is, up to 5 years after internal fixation. The prognosis as to the ultimate fate of the femoral head of a fractured hip, in this writer's opinion, is guarded under even the most ideal conditions. This author believes that the immediate fate of the femoral head may be sealed at the time of fracture by receiving irreparable damage to its blood supply but that this accident is relatively uncommon.

He believes, on the other hand, that the early fate of the femoral head is more often determined at the time of reduction. Further, he believes that one can predict with a certain amount of accuracy from the roentgenographic views taken at the time the fixation is done which heads will unite and live and which heads will not unite and will die. All failure in the series of cases to be shown had one fault in common. All hips that healed did not contain this fault. Not only in this series, but in all the author's experience, this has been the rule, not the exception.

Clinically, patients who are going to have good hips are well on their way toward this end by 5 weeks after fixation. Patients who are going to have poor hips at no time handle the leg well following fixation. Limp, groin pain, adductor spasm, lack of internal rotation, and lack of full active control of the limb are present in all of these cases to variable degrees. From the time of fixation until the final check up, these failures never do get along.

Three patients not shown here, all women, were seen because of groin pain on weight bearing and motion. X-ray pictures taken with both hips in complete internal rotation showed slight decalcification about the affected hip with a suggestion of a break in the cortical continuity of the calcar femorale. No history of trauma could be obtained. Within 2 to 5 weeks all of these patients developed typical femoral neck fractures on the affected side. It is my belief that not a few typical femoral neck fractures are pathological in nature and that these people fall as a result of their hips breaking and not that the hip breaks as a result of a fall.

Before the study to be reported was begun, various methods of obtaining reduction and internal fixation were used. Open reduction was performed on hips previously reduced in the operating room and proved by roentgenograms and on hips not previously reduced. Closed reductions were done in the operating room with the patients in traction and on a fracture table. Closed reductions were also done with the aid of the fluoroscope, the fluoroscopic table, and manual traction being used. Leadbetter's maneuver was carried out in many cases. The heel and palm test was tried along

From the Department of Bone and Joint Surgery, Northwestern University Medical School.
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Fig. 1 Soutter apparatus disassembled showing traction bars, traction strap and felt, special hitch strap, double block set, sheet wadding, and spring balance. This apparatus offers traction to above 100 pounds and at the same time allows flexibility and movement of the part. It has been found invaluable for reducing old dislocations of the shoulder, dislocation of the hip, slipped femoral epiphyses, and many types of fractures. For reduction of intra-capsular fractures, the patient is thoroughly anesthetized. The long traction bar is placed under the patient in the long axis of the body. The traction strap is placed in the groin and hooked to the head end of the bar. The sheet wadding is rapped about the foot and ankle on the affected side and then the special hitch strap is attached over this. The spring balance is hooked to the hitch strap by the iron rings provided in the hitch strap. The balance is then hooked to the double block set which in turn attaches to the foot end of the bar. Traction is applied with the leg in external rotation and about 60 degrees of abduction. From 60 to 80 pounds of traction, as read on the spring balance is applied. The operator stands under the knee and with the traction on gentle flexion of the hip about 30 degrees is done a few times. Then the knee is grasped and if complete internal rotation can be achieved by very little force reduction is probably satisfactory. When internal rotation occurs, the leg is then adducted by moving the Soutter bar toward the other leg. A small sand bag is placed under the knee to support it and prevent trial on the medial aspect which will result from the assistant's pressure. An anteroposterior roentgenogram is then obtained. If reduction is complete an assistant holds the position obtained without any change until the whole fixation procedure is completed. No frogging or motion of any type is permitted.

Fig. 2 The special instruments required for this procedure. Hammer, assorted nails, sizes 4 to 4 3/4 inches in length, and cannulated to accept 3/16 inch wire. Drill, the Jacobs chuck, Nail, wire and driver shown as unit. Guide as developed by Edward Geckler of Philadelphia and modified with his permission, to accept the wire instead of screws. Starter—this is used to incise the cortex of the femur before the nail is inserted. It is done by threading the starter over the wire and then by gentle tapping until the starter enters the cortex, then disengaging the starter from the femur turning it one-quarter turn, and repeating the procedure in this manner until the cortex has been softened. This avoids splitting of the cortex and the turning of the nail edges. In using the guide the sharp

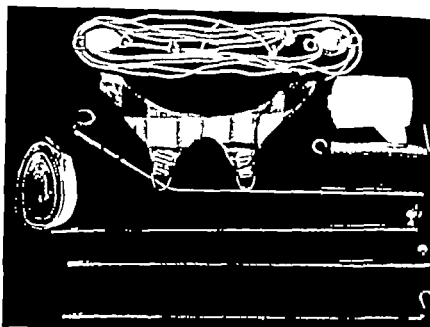


Fig. 1



Fig. 2

pointed long rod is pushed through the skin. (2) It hits the lateral aspect of the femur. It is then brought to the anterior surface of the femur and then by lifting up on the handle the point keeps in contact with the femur constantly as it is worked up until the head is reached. Then the point of the rod is firmly skewed into the head or acetabulum, as the case may be, to give firmness to the guide apparatus. The skin is incised, transverse incision, such long bone made at the point indicated by the guide handle. The sharp wire holder is thrust through the handle into the wound until it strikes bone, is fastened by the thumb screw, and the wire drilled home. This wire must be new with an excellent sharp point, or difficulty will be experienced in starting the retractor. Acute angle with the shaft. The nail is then threaded over the wire, after the cortex is macerated, it is tapped home, not driven with force. Small fast strokes, of little power are all that is necessary or should be done to set the nail. While this is being done, the fluoroscope room dark and the operator works by a red light handled by an assistant. Only the operator is specially gowned.

Fig. 3. a, The guide is in place, the guide rod has been rotated slightly to show the guide wire entering the proximal fragment. Note that internal rotation is complete and no sign of the lesser trochanter is visible in the film. Unless this is true, complete internal rotation has not been obtained. The small white area on the inferior surface of neck marks the long cortical line of the femur, the *calcar femorale*, the true line of weight thrust. Note that the guide wire enters the femur at or below the level of the lesser trochanter and runs roughly parallel to the *calcar femorale*. The guide wire is now run into the head to the depth desired and anterior and posterior lateral films are taken. If the wire is at the right depth, another wire of equal length is thrust by hand through the wound close to and parallel with the guide wire. This second wire will strike the femur. The difference in length of the two wires at the operator's end is the actual length of the nail required. b, Lateral view. Figure 4, a, showing guide rod and guide wire in position. The guide



Fig. 3a.

Fig. 3b

wire should be the proper depth if direct measuring of the nail is taken as described. Following measuring of the nail, good practice is thought is to drill the wire deeper a little into the acetabulum. This is an added factor in preventing a deviation of the head that might be caused by the nail as it enters the head.

with other devices. The conclusions after experience with these methods were as follows:

Open reduction. The chief value gained here was the ability to compare the actual findings in the hip with the findings in the preoperative roentgenograms. Thus developed a better roentgenographic interpretation of what constitutes a well reduced hip. The conclusions reached were (a) that any hip that can be well reduced without opening does not need an open procedure. (b) that the occasional hip in which reduction cannot be obtained while closed should be opened. (c) that if good contact between the head and neck is gained with no anterior or posterior angulation of the head on the neck and the neck well under the head fragment, the fact that the head fragment

may be rotated somewhat on the neck has no more effect on the healing than rotation following osteotomy for rotation deformity has on bone healing elsewhere in the body. (d) that if the hip is not reduced previous to open operation, this writer knows of no more difficult piece of hip surgery, with the possible exception of correctly reducing and fixing a slipped upper femoral epiphysis, than is encountered in correctly reducing and internally fixing a femoral neck fracture by the open route.

Closed reduction. The fracture table was used. This table offers certain advantages but with the stiff unyielding traction of post and counter pull the reductions were poor. Great strain was on the knee and all in all the plain wooden table with the cassette holder under its top and traction pro-



Fig. 4a.

Fig. 4b

Fig. 4c

Fig. 4. Shows nonunion of femoral neck fracture 1.5 years duration. This patient was operated upon by pulling shaft well down and then performing an intertrochanteric osteotomy. No attempt was made to freshen up the fracture site or to interfere with the capsule in any way. b, Same patient as Figure 4, a, 3 years after osteotomy. Patient walked without support 14 weeks following osteotomy. Four years after osteotomy condition of hip similar to patient leads active painless existence. Whether head is dead or not 4 years after operation joint space is maintained, head is of normal shape and previous union which was rapid, is present. Union occurred, as with fractures elsewhere, because weight thrust was direct, shearing and torsion forces avoided. Note internal rotation of shaft and amount of lesser trochanter that is visible. If the conditions existing here could be obtained in fresh femoral neck

fractures the possibility of prompt healing might be enhanced.

Fig. 5. Abduction type of intracapsular fracture. This type is impacted. These need not be fixed internally because most of them heal kindly. It is safer however to fix them—one feels more secure. Note almost complete internal rotation and degree of valgus of the head. Particularly note *calcar femorale* and that the neck fragment is under the head fragment. If settling takes place, the neck, by itself, will support the head in correct line of weight thrust. This is similar to what is accomplished by intertrochanteric osteotomy. Some so-called abduction type of fractures are not really this type at all. These readily fall to pieces. The same criteria used for determining adequately reduced abduction fractures can be applied in determining true or false abduction types.



Fig. 6. a, Adduction type of femoral neck fracture. Limb has complete external rotation. The complete disengagement of fragments. All hips of this series are of this type. b, Same patient as in Figure 6. Spot film taken at time of reduction. Note complete internal rotation. The absence of lesser trochanter. Note that neck fragment is under and inside of head fragment as judged by calcare femoralis. This simulates the position obtained by osteotomy. The head is in valgus. If great traction is not applied with the leg in internal rotation, it is difficult to get the neck by the head. Unless the neck gets beneath the head, complete internal rotation cannot be obtained because the neck fragment will hit the head, thus preventing reduction. Only anatomically or over-reduced fractures allow complete internal rotation. Once the above position is obtained adduction of the limb to neutral or slight adduction throw the head into more valgus and gets the neck farther to the inside of the head. The neck, not the fixation material, takes the eight thrust from the head. c, Same patient as in Figure 6, b, 3 years after fixation. The neck fragment can still be seen under and inside the head supporting it. The shaft is thus prevented from using the head as fulcrum and adducting and thus forcing the neck up and past the head to produce varus. In this case varus has occurred. Internal rotation is free in the direction of Smith-Petersen nail. It starts below the level of the lesser trochanter, runs parallel to the calcare femoralis. The nail is preferred because in a correctly reduced hip, the nail acts only as guide, which is a direct line of eight thrust and is only function is to deliver the head to the proper position on the waiting neck. The neck, itself, does the supporting the eight thrust the impacting.



Fig. 7. a, Spot film taken at time of reduction. Note that some abduction of shaft exists and that the neck is not truly under and inside of head fragment. This position is unsatisfactory. b, Same patient as in Figure 7 a, spot film taken after more traction. Internal rotation, pushing medially over the trochanteric region and adduction of shaft. Note change in valgus of head and that the shaft is now under and inside of head fragment. Position satisfactory. c, Same patient as in Figures 7 a, and 7 b, 5 months postoperative. Patient began weight bearing 5 months after fixation. Back to work full time without pain, limp, or support 9 months from fixation. Perfect clinical result to date.

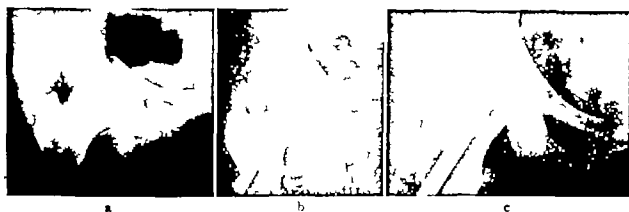


Fig. 8. a, Spot film showing reduction. Note that the neck fragment is well under and well inside of head fragment. b, Same patient as in Figure 8 a, 3 months after fixation. This patient was allowed full weight bearing at a time through a misunderstanding. Note position of nail. Note that as the shaft attempts to adduct in stead of exerting tremendous force on the fixation material, the neck fragment tends to thrust the head to more valgus by the leverage that is applied by the inner side of the neck to the head. c, Same patient as in Figure 8 a, 18 months after fixation. Note in region of calcar femorale that the neck is well under and in direct line of weight thrust.

vided by the Soutter apparatus was found the most satisfactory.

The safest method for the operator to adopt is blind nailing in the operating room without use of the fluoroscope. In this method the closer the dark room is to the operator the less fatiguing to all.

Manual traction. This method failed to gain adequate reductions in many instances. The heel palm test was found to be of little value in determining a reduction.

THE STUDY

There were 4 out and out failures in this group of 38 consecutive subcapital or transcervical fractures. Two of these failures are shown in the illustrations. The longest time from fixation in this series was 4 years and 8 months the shortest time was 18 months. The youngest patient was 35

years of age. The oldest patient was 90 years of age. There was 1 death the 90 year old patient died at the age of 102 years. All the other patients were living at the last check up. There were 5 males in the series. There were no infections.

No impacted (abduction) fractures and no basilar fractures have been included in this series. All hips in this series were completely displaced and subcapital or transcervical in location. All patients have had roentgenograms of their hips every 3 months the first year and every 6 months thereafter.

Repeatedly it has been stressed by various writers that a good reduction of a femoral neck fracture should have the head in valgus with good contact between the head and neck. This paper will attempt to standardize the criteria of what constitutes a good reduction and then to show that these criteria are present or absent in the spot

Fig. 9. a, Spot film at time of reduction. Note the poor position of head, full internal rotation of shaft but that neck is under and inside of head fragment. The head is in valgus and if the neck was not under and inside of the head fragment all weight thrust would be on the fixation material not bone against bone. If the shaft should then adduct the neck would readily slip by and up and in relation to the head. Compare with Figure 10 a. b, Same patient as in Figure 9 a, 2 years after fixation. No limp, no support, full motion and no pain. Head has united in peculiar position but union has occurred. Note that the neck is well under and inside of head in region of calcar femorale supporting the head. All nails, with but two exceptions, have been left in place in all cases except the four failures. The 2 cases in which they were removed was because in 1 case the nail was too long originally and gave pain in the soft tissues. The other case is illustrated in this article and the nail came



Fig. 9a.

Fig. 9b.

partially out. In all other cases, except the failures, the fixation material did not abut.



Fig. 6. a, Spot film at time of reduction. Note lack of internal rotation and in this case conditions are reversed and the head fragment is below and inside the neck fragment. In this instance adduction of the shaft on the head is allowed because the neck fragment does not support the head. Compare with Figures 8, a, and 9, a, b. Same patient as in Figure 5. a, 6 months after plating. Note that slight adduction which puts head into more varus. Nothing is supporting head except fixation material. Varus in these cases is produced by adduction of the shaft. If the head fragment is below neck fragment adduction and angulation is permitted. If the reverse is true, the adduction is prevented by the neck fragment supporting the head and angulation cannot occur and weight thrust is delivered solidly against the head with no shearing or angulating forces able to act effectively. c, Same patient as in Figure 5. a, 9 months after fixation. This is not an end result but it has gone to complete failure. Note density of head. Note how the head has been passed by the neck as adduction of the shaft occurred. The effect of this force is well illustrated in the flight of the screws. Any of the numerous fixation gadgets will probably hold properly reduced fracture because no real strain is upon the fixation material. On the other hand, no material will hold in movable cancellous bone when shearing and torsion forces take effect. The material either breaks, migrates, or becomes loose because the force is not bone against bone but metal against bone, impossible mechanical and physiological set-up. It is, therefore, not very important what force is necessary to break or distract gadgets put in hips. If the gadget acts as a guide line with weight thrust, allowing the head to settle on the neck with the force transmitted properly from head to neck, very little holding power is necessary; only rotation must be prevented.

The Smith-Petersen pin allows strength, rigidity, and being in one piece acts as an ideal guide. The nail itself has no effect on blood supply to the head, and in these cases the nail has not been removed except as noted and no ill effects have occurred. There are no nail blood vessels in the center of these femoral necks and heads, except sclerotic ones near the fovea. Compare with Figure 5. a.



Fig. 7. a, This case not the 'thor' and is not included in this series, but it is shown because of result. Note reduction with fall of neck fragment to be under and inside of head fragment. Fracture is quite low on neck, almost basilar. Not adequate internal rotation. Not placement of fixation material. Note valgus position of head. Compare with Figures 7 and b, b. Same patient as in Figure 6. 6 months after fixation and at time eight bearing was started. Typical of all failures—internal rotation was lacking, groin pain, adductor spasm and limp with support were present, but mild. c, Same patient, 3 months after fixation. Note adduction of shaft, and how the neck has moved up farther in relation to head which is in varus. Nothing supports head fragment. Note density of head and production reaction. This is classed as failure. The movement of the unsupported head and shaft is what breaks the metal or sends it into the pelvis or works it out of the head. Compare with Figure 7.



Fig. 12 a A spot film at the time of reduction. b One year since fixation. c Two years since fixation. Note marked obliquity of fracture line. b One year since fixation. Note external rotation of shaft and that the nail has been extruded. Note that shaft has adducted but that the head fragment is in place. Patient at this time is walking without support. c Two years since fixation. Note union present. Patient in full control of limb except internal rotation limited to neutral. Full normal activity. No pain except when lying on affected side when nail is bothersome. No support. Slight hesitancy in gait but no limp. One-eighth inch heel raise on affected side and one eighth inch off heel on normal side balances for good gait. Estimated as a good but not an excellent result. Compare with Figures 4, b and 13 d. Note increase in internal rotation between time of Figure 12 b

films taken at the time of reduction. If the criteria at the time of reduction are satisfied the results will tend toward the excellent. On the other hand if these standards are lacking at the time of reduction failure will result in many more instances than otherwise. In these failures non union fibrous union, aseptic necrosis extrusion of fixation material shortening and deformity will be commonplace. The changes in the head and neck that indicate impending failure of hip fixation were found to be present in the roentgenograms within the year from the time the fixation was done.

THE ROUTINE

At the time the fracture was first seen Russell traction was applied. The patients were encouraged to move about lift themselves up and down to sit up to roll and in all ways to keep moving. These fractures were not considered emergencies. It was felt rather that good medical care the preoperative activity and time to size the patients up were important adjuncts in improving their chances.

All patients were turned from back to sides every 2 hours by the nurses. Involuntary pads were placed under them and all effort was made to keep these people clean and dry. If rubber sheeting was between the mattress and sheets, it was insisted upon that a mattress protector be placed

on top of the rubber sheet and then the bed sheets over this. By this method pressure sores were not encountered. If it was not insisted upon that each patient turn herself or was turned every 2 hours the floor care was desultory and the patient became wet developed excoriations and bed sores. The nurses would only notice trouble and remedy it if the patient was turned. If the patient was not turned good back hygiene was usually lacking.

In about 10 days if the patient was active and comfortable the operation was proceeded with. In this series the routine premedication was $1/12$ th grain morphine and $1/150$ th grain atropine. No morphine after surgery was allowed. Pentothal sodium was used in all cases for induction and relaxation. After reduction the pentothal was either discontinued or a slow drip was started and the patient was carried on a mixture of 60 per cent nitrous oxide and 40 per cent oxygen. This combination was the most satisfactory type of anesthesia we have tried. It is in our hands far superior to spinal or local anesthesia. Spinal anesthesia produced various types of reaction and local anesthesia failed to give enough relaxation.

All reductions and fixations in this series were done on the fluoroscopic table. The fluoroscope had a spot film attachment but this is not an absolute essential. The portable x ray unit was used to obtain the lateral views.



Fig. 3. a, Spot film, time of reduction. Patient woman, 54 years of age. Not ability of fracture line and complete internal rotation. The neck fragment however fails to be below and distal of the head fragment. There is no bony support to prevent shearing thrust. Compare with Figure 1. b, Hip 6 months after fixation. Not complete internal rotation of neck of nail and that head fragment be seen tend to be distal of the neck fragment. The fracture at other side appears to be union. Weight bearing started at this time. Compare with Figure 1. c and d, One year since fixation. Not complete internal rotation. Nail remains in position. Not distraction of shaft and relation of shaft to head. Productive reaction about fracture site. Fibrous union, though not preventing shearing forces, work against the supported

head. All support is being taken by the nail and not by the femoral neck. Patient at this time is walking with minimal limp, uses cane and has pain in groin with adductor spasm and some flexion deformity. Unable to do housework without pain but is active. Full active control of limb has been obtained 1 year since fixation. Not changes in and about femoral head. Internal rotation still present. Nail remains in position. Not adduction of hip. Patient was once, lacks full active control of limb, has pain and marked limp but does housework with difficulty. This is failure. At the vascular and productive changes seen in this and other failures due to the original trauma or are they the result of poor mechanical set-up resulting in chronic irritation and altered physiology. Such nature reacts by attempting to pull the offending part off and sequestrate it?

The fluoroscope was used to introduce the guide. This step took but a few seconds and once the guide was correctly placed all checking by the operator was done from roentgenograms.

The roentgenologist or a technician trained in this work handled the fluoroscope and the taking of the x-ray films. This arrangement eliminated wasted time, minimized the exposure of the operator, and enabled him to work efficiently with

out contamination or bother. The judging of the depth of the guide wire and the depth of the nail along with the taking of the films all were supervised by the person operating the fluoroscope. The operator checked these observations in the roentgenograms. The time to complete the whole procedure from reduction to wound closure was from 60 to 90 minutes. About 20 minutes of this time was consumed by the actual operation.



Fig. 4. Spot film, lateral view of reduced fracture. This view shows back and tilting of head because not enough internal rotation has been produced. Split of the disappearance of the major portion of the lesser trochanter in the anteroposterior view. The guide wire enters the head in the anterior portion, but centers the neck. By gentle manipulation, all internal rotation possible has been gained. To correct this position, the Smith-Petersen nail is threaded over the guide wire and is gently driven into the neck to depth, approaching the fracture line. The guide wire is then

drilled out of the head until its point is hidden by the nail. The nail driver is then reattached by threading it over the wire and screwing it into the nail. Using the driver handle as a lever, internal rotation is easily increased to the desired amount. The knee is held in the new position by the assistant. The guide wire is driven into the head again and anteroposterior and lateral views are obtained. If satisfactory the nail is driven home. X-ray films again check the final result. b. Same case after procedure described in Fig. 4, a, has been completed.

No hip can be considered internally fixed until perfect anteroposterior and lateral views have been taken proving without doubt that the fixation material is well centered of proper depth that no twisting or angulation of the head has occurred and that proper reduction is maintained in both planes. So important is this one point that no hip should be internally fixed where an excellent clear lateral view cannot be obtained.

All figures in this article and all patients in this series had excellent lateral views showing the fixation material engaging the head in a satisfactory manner. It was not enough to have the view showing the guide wire in correct position. In these views were repeated after the nail had been driven home. While the nail was being tapped home the roentgenologist viewed its progress at times while the operator stepped away. This was done so as to avoid the nail catching the wire and driving it ahead toward the pelvis. If the wire did move it was drilled farther in or out as the case required so as to prevent the tip of the nail from engaging the bent portion of the wire.

To date this writer has never had a shaft or head split or fracture from the introduction of fixation material.

Following operation the patients were again placed in traction. The patients were required to sit up, roll, and to be turned every 2 hours. They were encouraged to lift themselves about in bed with the aid of the cross bar dropped from the Balkan frame.

No attempt was made to hurry these people out of bed. If as in all of this series they did well in bed they were kept down from 3 weeks to 12 weeks depending upon their age size and ability to handle themselves. Exercises such as deep breathing, leg and arm movements were given. Daily physical therapy to the knees and feet in the form of massage and exercises was started about the fourth day after fixation. Weight bearing was started from 4 to 6 months after fixation. No braces or calipers were used.

From both the mortality and morbidity standpoint this author has had far more trouble in people with fractures about the trochanters than he has experienced with the group presented here.

The illustrations are used to emphasize the principal points brought out in this article.

SUMMARY

The suggestions for standardization of what constitutes adequate reduction of intracapsular femoral neck fractures are presented.

These suggestions are the result of studying numerous roentgenograms over a 6 year period and

of attempting to find certain characteristics which were present in those roentgenograms in cases that were successful but which do not obtain in roentgenograms of cases that were not successful.

The method described for obtaining reduction of femoral neck fractures is based on complete relaxation under an anesthetic and then pulling the limb down in external rotation and slight abduction. While the traction is on, gentle flexion and rocking of the hip is carried out until the neck passes the head. The limb is then internally rotated to its limit. No resistance should be felt in carrying out this maneuver. The patella should be directly medially and the internal femoral condyle should be directly on the small sandbag that supports the knee. When this position is obtained the limb is adducted to neutral or slightly beyond. An anteroposterior and if desired a lateral film is now taken.

If in the anteroposterior view the criteria are satisfied the guide is inserted, the guide wire is put in, and anteroposterior and lateral views are now taken. If the wire is perfectly centered in both views and the hip is reduced in both views the nail is driven home. Anteroposterior and lateral x-ray films check the depth and position of the nail and the reduction. If these are satisfactory, the guide and guide wire are withdrawn and the wound is closed.

The technique described here for fixing hips internally is not advocated but is described to illustrate certain points.

The reduction is applicable to the operating room and a flat wooden table with a cassette box under its top proves as satisfactory as any table. The Soutter apparatus has been the most satisfactory method of applying traction.

All standards described in this paper are based on roentgenograms taken with the limb in full internal rotation. In this way the neck length is established. If the roentgenograms in this paper are studied one will note that the head and neck are separate from one another and there are no overlapping shadows where a portion of the neck covers a portion of the head. If overlap is present, it means that a complete reduction has not been obtained because if complete internal rotation is present any overlap indicates overriding or angulation, but not end-to-end contact. Any x-ray view short of complete internal rotation distorts the relationship of the head and neck and makes interpretation of the film practically worthless.

A satisfactory reduction is one in which the limb is in complete internal rotation and at least neutral lateral position. The neck fragment is well under and well inside the head fragment as

shown in the anteroposterior view. In the lateral view the head and neck are in line with no angulation and no overlap. The fracture surfaces are apposing one another.

A satisfactory fixation is one in which the fixation material enters the shaft of the femur at or below the level of the lesser trochanter, runs through the lower one-half of the neck parallel to the calcar femorale, and centers the head in both planes.

The main purpose of the fixation is to act as a guide which allows the head to settle on the neck in a position in which the weight thrust is directly applied to the fracture site without shearing or torsion forces being exerted on the fixation material. The position that the femoral head and neck should assume to gain this objective has been described.

CONCLUSION

This author does not wish to insinuate that there are no failures in a comparatively large number of hips that have been internally fixed since the series reported here was closed. He has had failures, but the point he wishes to stress is that all

the failures have occurred in hips that have been imperfectly reduced. That is, the neck fragment has not been placed well under and well inside the head fragment.

These failures have been due to many factors such as inability to obtain correct traction, inability to obtain adequate lateral roentgenograms, poor anesthesia, personal carelessness, and occasionally inability to obtain satisfactory reduction of the hip under ideal conditions.

In closing, an appeal is made first, for the fixation of hips in a place where all factors are in the patient's and the operator's favor; second, that a hip cannot be reduced or if there is doubt as to the effectiveness of reduction, either an immediate intertrochanteric or a subtrochanteric osteotomy be performed as the case may require; and, third, that if a hip is fixed but is not doing well, at the first signs of failure an osteotomy be done.

If a plan similar to the above is carried out it should aid in reducing the amount of disability now following intracapsular fractures of the femoral neck.

SUPPORTIVE IMMOBILIZATION OF THE CERVICAL SPINE

EDWIN BOLDREY, M.D., San Francisco, California

SUPPORTIVE immobilization of the cervical spine following a period of skeletal traction or when such traction is unstable or contraindicated has been an annoying neurosurgical and orthopedic problem the attempted solution of which has brought forth numerous devices of varying merit. The cast or splint is built up beneath or around the chin to such a degree that eating is greatly interfered with if the jaw is permitted movement. There is likewise movement in the cervical spine. The result has been a failure to support or to immobilize or both. Cone¹ circumvented this difficulty by a plaster-of-Paris cast which encircled the forehead and from which reinforced prongs extended forward beneath the ears to lie along the maxillary arch below the zygoma. The cast then extended over the neck posteriorly and laterally and was continuous with a body jacket. The mandible and throat were entirely free. Sometimes

the auxiliary prongs were connected over the bridge of the nose.

The disadvantage of this apparatus lay in its weight and in the difficulty in maintaining the satisfactory position of patient and plaster during the process of setting. A further disadvantage shared by all methods employing plaster is that the means of immobilization after skeletal traction for fracture, dislocation, or fusion of the cervical spine is the tendency for syncope to appear when the patient sits up as is usually the case. It is almost necessary if a properly fitting cast is to be applied.

It appeared that the unsatisfactory aspects of the Cone type of cast might be avoided by a properly fashioned brace and the following plan was drawn up. It calls for an aluminum cup molded to the occipital and suboccipital region and projecting laterally, partially encircling the ear. This cup is attached by steel bars to padded spinal shoulder and trunk bars. From the supra-auricular part of the cup a broad webbed strap connected by buckles to similar webbing padded with felt holds the head firmly in the cup and helps to

From the Division of Surgery, University of California Medical School, San Francisco, California.
Dr. W. V. Cone developed this cast several years ago at the Montreal Neurological Institute.

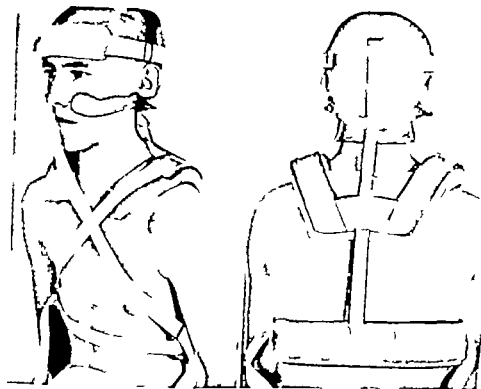


Fig. 1. Front and rear views of apparatus.

eliminate flexion-extension movement. From the infra auricular part of the cup and connected by a ball and socket (universal) joint a prong made of aluminum molded to the contour of the maxillary and infrazygomatic region is carried to the vicinity of the nasolabial fold. This prevents rotation and further impedes flexion or extension of the neck. The whole is covered with soft leather. Shoulder and trunk braces are stabilized by buckled webbing.

This proposal was outlined to Mr. Gus Kern, brace maker for Children's Hospital in San Francisco, who then constructed the splint shown in the illustration (Fig. 1). The patient for whom it was tailored was a boy of 17 convalescing after a fracture involving the atlas and axis which had been treated by skeletal traction with Crutchfield tongs. Fittings of various parts of the splint were carried out with the patient still in traction and in bed. The splint was applied while he was recumbent so that he had immobilizing support when he first was brought into the erect posture.

The effectiveness of any device to prevent movement is determined to a large degree by the one employed by the brace maker in fitting it to the individual. In this case there was no observed movement of the patient's cervical spine, either when chewing movement or when voluntary cervical motion was attempted. The patient reported the splint to be comfortable. He wore it continuously night and day for a period of 6 months without objective or subjective evidence of difficulty.

Though occasion has not yet arisen, it is believed that the brace could be sufficiently standardized to serve as a splint for emergency transport after injury to this region. Its advantages over Wagoner's² splint are its design primarily for cervical fracture, and the infrazygomatic splint which provides additional stabilization. For satisfactory convalescent supportive immobilization, however, an individually tailored brace will continue to be necessary.

Wagoner, George D. *B. Naval Med. Bull.* 925, 20: 390-394.

EDITORIAL

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THE RÔLE OF THE SPECIALIST IN MILITARY MEDICINE¹

THE rôle of the specialist in military medicine has always been a vexing problem. Quite naturally the tendency among military men is to feel that all military physicians must be ready to meet any and every medical or surgical emergency which might arise on isolated posts and that consequently every military physician must be a general practitioner with a high degree of specialized skills. There can be no doubt that the level of all around specialized medical knowledge which has been achieved in the medical services of our Army and Navy is of a high order higher indeed than is true for the average general practitioner of civilian life.

This is a great achievement yet, it would be shortsighted to allow an analysis of the problem to stop at this point. One still must ask whether in addition to this body of highly trained general practitioners of military medicine the armed forces do not need the

practical skills and the scientific leadership of the highly trained specialist. If so organizational plans must solve the following problem: (1) how to attract specialists into the armed services (2) how to give those military physicians who want to become specialists an opportunity to develop in this direction (3) how to hold such men when trained in the armed services and (4) how to plan the relationship between the specialist and the general practitioner in the armed services.

The pros and cons of these problems have recently been presented in an article entitled

The Problem of Specialization in the Medical Services of the Regular Army and Navy Prior to the Present Emergency.² This article presents statistical data which indicate that prior to the present emergency the representation of the medical departments of our armed services was very low in national medical and scientific societies and among the diplomates of our specialty boards.

It seems apparent that the existing tendency to try to make of every military physician a general practitioner while understandable has two drawbacks so serious as to overshadow any advantages. In the first place it makes it difficult to induce and attract men of top flight ability to make a life career of military medicine. (If anyone doubts this let him consult the records of our best medical schools for the last twenty years and see how many of those who graduated in the upper quarter of the class entered the regular Army or Navy medical departments.) In the second place it results in confusion, loss of time and loss of efficiency whenever an emergency arises.

²Bull. New York Acad. Med., 44: 20 Sept.

¹This editorial was written by Dr. Noble at the request of the Editors.

In this war as in World War I there was an initial period of fumbling and uncertainty which lasted for about two years before the civilian specialist was used according to his specialized skill and training. At first there was an abortive effort to make of every specialist a general practitioner. Gradually this petered out and the offices of the Surgeons General of the Army and Navy were reorganized into a pattern that approximates more closely that of a well run medical school or general hospital with divisions representing each relevant specialty usually under the leadership of civilian specialists. Because of the late date of such reorganizations however it has never been possible to alter the Tables of Organization of medical installations completely enough to give the specialties effective representation through the lower echelons. The start in this direction is only under way as the end of the emergency approaches. Furthermore immediately after the last war the pendulum swung back, most of the specialty divisions were dissolved and the Surgeon General's Office returned to the prewar nonspecialized organizational plan and policy.

It is our contention that this should not occur again. Our national societies and our national specialty boards thus seem to have a manifold duty. (1) They should maintain close permanent liaison with the offices of the Surgeons General of the Army and of the Navy. (2) They should encourage among their own membership the organization of Army and Navy specialist reserve corps as active units with periodic tours of training with military units and periodic refresher courses. (3) They should urge and support plans for a permanent organization of the Surgeon General's offices along lines which will permit representation of all relevant

specialties with correlated changes in Tables of Organization from the highest echelon down as far as is necessary into the lower units. (4) Above all our national specialty societies and our national specialty boards should use their prestige and authority to make sure that young medical officers, who have the aptitude and the desire to become specialists should have the opportunity to make careers as specialists within the armed services, with opportunities for specialized clinical experience and for research and teaching in their special fields.

Our position cannot be better summarized than in the words of the late Thomas Salmon as quoted in the article already referred to.

I imagine that there will be no dissent from the statement that the regular establishment needs to have the important specialties adequately represented at all times in its own personnel. If there were no other reason the retention of young medical men who enjoy military life but who would leave the service if not permitted to work along the lines of their special interests would be sufficient, in the present shortage of medical officers. Unless special, as well as general, tasks in military medicine are systematically and skilfully taken it will be useless to expect regular officers who will occupy high administrative position in war to know how to use specialists to the best advantage. Hostility or at least skepticism will be their attitude if they are thrown into contact with those working in special fields with no previous association as a basis for mutual understanding and respect. It is equally important that specialists should know how to work in the Army. Many a highly trained specialist from civilian life was less able to apply his skill to the actual problems of military medicine because he insisted upon conditions that could not possibly exist in a military organization.

This was the wise advice of a specialist who never in his civilian career had been narrowly specialized who had exceptionally wide experience in co-ordinating the work of general practitioners and specialists in the problems of civilian medicine and who saw service in our army throughout the years of the last war as chief of the psychiatric division.

LAWRENCE S. KUBIE

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REVIEWS OF NEW BOOKS

THE comprehensive treatise by Adam entitled *Intravenous Anesthesia* consists of a review of all the available literature on intravenous anesthesia from its inception until the present time of all the drugs that have been administered intravenously to produce anesthesia, the various methods employed and the results obtained. The volume is so arranged that it can be used readily for reference work. The chemical and pharmacologic aspects of the drugs are discussed in detail and separately from the clinical aspects. The discussion of the clinical effects includes a consideration of the use of the drugs in special fields.

Each chapter and the discussion of each agent are subdivided into four main sections: history, chemistry, pharmacology, and clinical use. The sections regarding clinical aspects are further subdivided into discussions on the use of the various drugs in surgery, medicine, obstetrics, psychiatry, and so forth. Each chapter has its own set of references with an extensive bibliography, thus making the book suitable for reference work.

Attempt has been made to have the nomenclature conform with the chemical and pharmacopoeial terminology as approved by the Council on Pharmacy and Chemistry of the American Medical Association—a task particularly difficult because of the great confusion now present in terminology.

The foreword is written by John S. Lundy, and a constant reference is made to him, whose preliminary work, intimate knowledge, and enthusiasm for this subject have helped elevate intravenous anesthesia to its present position. The chapter on the historical considerations is detailed and complete.

The various agents which can be administered intravenously to produce anesthesia have been classified in tabular form, and include volatile and non-volatile agents, local anesthetic agents, the urea derivatives, the inorganic salts, narcotics, hypnotics, and barbiturates. Each agent is discussed separately in detail in the following chapters, the advantages enumerated, and the experimental clinical work with them recorded. The author's wide experience and excellent manner of presentation make his description of the technique of intravenous injection interesting. A set of illustrations show the various techniques of administering pentothal and the apparatus now available.

The chapter on evipal sodium carries the most extensive bibliography, including 482 references and 236 relevant articles not referred to in the text.

By R. Charles Adams, M.D., C.M.
New York and London: P. B. Hoeber, Inc.

The chapter on pentothal, however, presents most of the author's own investigation and data and it is both most detailed and complete. Pentothal sodium at the present time offers the optimum as a close to total intravenous anesthesia. The chemistry, in vitro and in vivo, the manufacture of the agent, its effect on the various systems of the body, the pathological changes involved, and its clinical application are discussed in detail. Also are the preparation of the patient, preliminary preparation of the drug, and the technique of administration. A table of the signs of an overdose produced by a 2½ per cent solution of pentothal sodium is interesting and can be used to great advantage for teaching purposes. A detailed discussion is presented of the untoward effects and all of the complications, indications and contraindications, and military applications. The bibliography is extensive and complete.

A chapter is devoted to the analeptics and another very excellent chapter to the military surgical application of the intravenous anesthesia.

Intravenous Anesthesia is an extensive detailed report on all of the data available pertaining to the subject. It is a reference book which can be well utilized by the student of anesthesiology as well as the investigator interested in research. The compilation of the volume must have involved years of work and study. Its publication is welcomed by the specialist in anesthesiology; it brings up-to-date a subject whose life span is only a few decades and whose future must certainly be considered as an integral part of the future of anesthesia.

MARY KARP

PLANNED timing in the treatment of wound is particularly borne out in the motif of the book *Technique in Trauma* by Fraser B. Cudd and I. Douglas Ackman. The book is very short and consists of three sections covering 60 pages and has numerous illustrations.

In the first section the authors review the principles of the treatment of burn and explain their conception of the principles upon which successful management should be based. They emphasize timing in treatment to anticipate the dangers and difficulties arising during the different periods associated with severe burn, namely shock, toxemia, sepsis, and repair. The general measures employed to anticipate and prevent shock, toxemia, and infection are principally those which have been emphasized in other recent articles. The local measures are advocated for the

By Fraser B. Cudd and I. Douglas Ackman, M.D., C.M.
New York and London: P. B. Hoeber, Inc.

prevention of infection and the promotion of rapid healing without formation of contractures include gentle cleansing of the wound with soap and water, the removal of debris and devitalized tissue, the employment of pressure dressings incorporating curtain drainage and a 5 per cent oil in water emulsion of sulfathiazole, and the early grafting of skin.

In the second section over 200 major and minor burns were reviewed and from this group 100 major cases requiring hospitalization were selected for analysis. Eight six of the cases had 30 per cent or less involvement of the body surface and 14 had more than 30 per cent. With the method of treatment advocated 6 of a total of 7 deaths occurred in the 14 extensive burns.

Short discussions of various subjects are included such as the assessment of the damage produced by the burn, the value of sulfonamide treatment, reconstructive grafting, and the treatment of anemia and hypoproteinemia.

In section 3 a similar plan of timing in the treatment of wounds other than burns is presented. This treatment consists of the application of efficient first aid and débridement, surgical antiseptics, occlusive dressings, changed infrequently, and rest.

Although the authors used no controls in determining the prophylactic value of local sulfonamide therapy, they have a profound impression that the addition of 5 per cent sulfathiazole in an oil in water emulsion gives an important additional safety factor against invasive infection and provides a medium for adequate curtain drainage. No invasive infections were noticed and the control of pre-existing infection was prompt and satisfactory. On the other hand they do not believe that sulfadiazine administered generally is indicated in severely burned patients except for unusual complications. In the opinion of the writers it may produce a grave and unnecessary risk to the liver and kidneys at a time when toxic manifestations from the burn itself are imminent.

Throughout the book the authors emphasize the importance of adherence to basic physiological and surgical principles and the application of these prin-

ciples by the use of planned timing and teamwork. Clear-cut and controlled evidence is needed, however, to demonstrate the value of sulfonamides administered either locally or systemically in reducing the incidence and severity of infection developed locally in burns or other wounds.

W. A. ALSTROM

IT is impossible in a few paragraphs to present an adequate review of Dr. Bunnell's *embrace*, a treatise on the surgery of the hand.¹ His book represents the work of a surgeon's lifetime—of painstaking and persistent application through many busy years to the problem of refashioning and restoring injured hands. This task involves many of the fundamental problems of surgery—the healing and repair of soft tissues, of tendons of nerves, of bone, the transplantation of skin and subcutaneous tissue, of tendons and nerves, the prevention and control of infection, the treatment of tumors, both benign and malignant—to mention only the outstanding ones. The problem as a whole involves a complicated and important mechanism whose function depends primarily upon the integrity of its parts and upon their freedom of movement. To secure restoration of function in such a mechanism after extensive destruction of tissue has occurred and after partial or complete fixation of structures that should move more fully has taken place requires infinite patience, imagination, skillful technique, and plain hard work.

No one can doubt in studying Dr. Bunnell's book that he has brought all these in full measure to the performance of his task. He has told and depicted with skill and imagination the problems he has faced, the treatment he has evolved, and the results he has obtained. Every surgeon who is interested in the surgery of the hand has been awaiting the opportunity of consulting and studying a comprehensive treatise such as Dr. Bunnell has prepared. We are indebted to him and grateful for this splendid contribution.

SAMUEL L. KOCK

SURGERY OF THE HAND. By S. Bunnell, M.D., Philadelphia, London, and Montreal: J. B. Lippincott Co., 1944.

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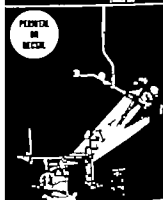
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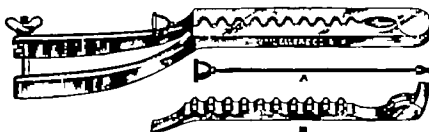
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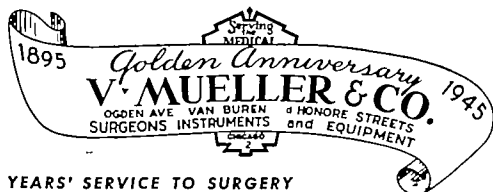
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REFERENCE: *Surgery, Gynecology & Obstetrics*, issue of December 1944, pp. 629-641. A Technique of Aseptic or Closed Gastric Resection Using the Furniss Clamp.

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Fig. Endometrioma of bladder wall showing typical gross appearance of a chocolate cyst.

Endometriosis of the Bladder and Ureter
— Vincent J. O'Connor and J. P. Greenhill

SURGERY

GYNECOLOGY AND OBSTETRICS

An International Magazine, Published Monthly

VOLUME 80

FEBRUARY 194

NUMBER 2

ENDOMETRIOSIS OF THE BLADDER AND URETER

VINCENT J. O'CONNOR, M.D., F.A.C.S. and J. E. CRIENHILL, M.D., F.A.C.S.
(Chicago, Ill.)

"Endometriosis is but a recent development of hystero-genital pathology" (Goodall)

VESICAL endometriosis was first described by Judd in 1921 under the title Adenomyomata presenting as a tumor of the bladder. In recent years with an increasing knowledge of the pathology of this condition the terms endometriosis, or endometrioma have been largely accepted as the common denominations.

It would appear that vesical endometriosis is always secondary to pelvic endometriosis that has extended into the bladder from affected contiguous organs. It is presumed to be a relatively rare complication as indicated by the fact that only 58 authentic instances have been recorded in the literature.

The origin and pathogenesis of endometriosis remain a matter of unsettled discussion. In general there have been three main theories advanced. The first and oldest suggestion made by von Recklinghausen in 1896 was that endometriomas arise from inactive embryonic rests derived from remnants of the wolffian and muellerian ducts. The second theory proposed by Ivanoff and Meyer was that due to some hormonal or inflammatory stimulation, the endothelial cells of the peritoneum

undergo metaplasia and assume the characteristic of endometrium. The third explanation is that endometriosis takes its primary origin from the endometrium and *always* from the endometrium. This latter theory has been most forcibly presented by Goodall in his recent monograph on this subject.

Sampson in 1921 and again in 1925 elaborated the spill and implantation theories. He contended that during menstruation and possibly during the intervening period uterine contents *escape* from the abdominal openings of the fallopian tubes and that in the spill there are living cells not only capable of implanting themselves but also in suitable tissues of reproducing the menstrual cyclic changes concurrently with the uterine menstrual phases. He further demonstrated the extension of outgrowths from the endometrium into the submucosal lymphatics and blood vessels in the form of emboli.

Marshall has recently reported the very rare if not previously unknown occurrence of an endometrial cyst within the left kidney. The patient was 40 years of age and complained of swelling and pain in the left flank for a period of 16 months. There had been no relation between the menstrual cycle and the severity of symptoms. Because of the complete absence of any evidence of pelvic pathology and the fact that there was no involve-

From the Urological Departments of Northwestern University Medical School and the Wesley Memorial Hospital.

ment of peritoneum Gerota's fascia or the renal capsule Marshall's opinion is that this lesion resulted from the inclusion of early muellerian cells in the metanephros.

Invasion of the bladder by endometrial tissue may result in the formation of single or multiple tumors which vary in size from a small pea like excrescence to a bluish black cyst several centimeters in diameter. The endometrial glands are scattered throughout a highly cellular stroma which is contiguous with the surrounding muscle bundles. The glands are composed of low to high columnar epithelium and in some areas the cilia of the epithelium may be discernible.

Moore Herring and McCannel have recently presented a thorough critical analysis of the literature on endometriosis of the bladder. Their review considered 46 cases. We have found 12 additional instances reported. The purpose of this paper is to present recent experiences of our own and to emphasize that continued search for and recognition of these lesions will probably prove that they are not the clinical rarity now supposed.

Thirty five of the patients with vesical endometriosis had had previous pelvic surgery before the discovery of the bladder involvement. Multiple previous operations had been performed in several as was the case in our patients. *In 7 of the 58 patients studied the endometriosis was supposedly confined to the bladder and no intra-abdominal pathology was noted.* The tumor was palpable on vaginal examination in one half of the cases. Description of the mass varied from an almond to that of a small orange in size. When present the palpable tumor is usually tender and vaginal pressure upon it may reproduce the discomfort which caused the patient to seek relief.

Subjective bladder symptoms are variable. Some type of cyclic disturbance was recorded in only two-thirds of these patients. The most constant symptom seems to be a sense of pressure or weighty discomfort in the vesicovaginal region. In some cases this was partially relieved by voiding but in others the pain was constant. Dysuria frequency and urgency are reported but no definite pattern of symptoms is described. Gross hematuria occurs

much less frequently than one would expect. It was noted in less than one-third of the patients. The cyclic discomfort, which in the main was most apparent for from 2 to 14 days of each month, was not characterized by a definite menstrual association.

The cystoscopic appearance of endometriosis of the bladder may or may not be similar to the appearance of a chocolate cyst of the ovary. In many instances the mucosal changes have been reported as definitely cyclic in character. The mucous membrane is elevated and the tumor is usually markedly congested and edematous. Often the cysts are translucent but more often have a bluish or blue black cast. The tumor is often larger during menstruation and less cystic during the intermenstruum. In other instances the appearance is not unlike that of a chronic inflammatory lesion or an early area of infiltrating carcinoma.

In our patient with vesical endometriosis the cystoscopic appearance of the lesion was so typical as to leave no doubt as to the cellular nature of the invasion. Cystoscopic biopsy of these tumors has been reported in only a few instances. On only 5 occasions was the diagnosis satisfactorily made by microscopic study.

Even though the endometrial nature of the tumor is not usually recognized and the tissue changes are described as those of chronic inflammation cystoscopic biopsy when possible is recommended to rule out evidence of malignant degeneration.

Goodall considers endometriosis a product of our civilization in that late marriages and still later conceptions are the rule owing chiefly to economic stress. Ovaries afflicted with endometriosis are in his opinion unusually prolific, filled with ova, and with the product of developing matured and defective follicles.

In the treatment of endometriosis, the problem is how best to effect a cure with the least amount of mutilation not only physical but functional. For the inception of all types of endometriosis, the ovaries are essential organs and their continued function keep up the activity of the disease. Removal of the ovaries or the arrest of their function by natural or

artificial means usually causes an abrupt ending of the disease. Occasionally removal of the ovaries does not arrest the disease. Such occasional cases have been reported which suggest that the tendency to infiltrate had gone beyond and become independent of the primary agency that initiated their abnormal reproduction.

In selecting the treatment of choice one must be guided by the age and condition of the patient and the extent of endometrial invasion in the pelvic organs, the bowel, the bladder, and the ureter. In younger women where one should make a sincere effort to preserve as much ovarian tissue as possible, localized excisions of involved areas should be practiced. Unfortunately in these patients recurrences are not uncommon and further surgery may be necessary to effect a permanent cure. Roentgen irradiation of the ovaries or castration, in women approaching the menopause should usually be followed by disappearance of the bladder involvement. In some instances the urinary tract lesion has persisted and even progressed after all demonstrable evidence of remaining ovarian tissue has been lacking. In these patients segmental resection of the bladder wall is not only indicated but may be imperative to prevent occlusion of the ureter by contiguous invasion.

Transurethral fulguration apparently has no place in the successful treatment of vesical endometriosis. An exception to this statement would seem to be the necessity for palliative treatment in an individual approaching the menopause. Large doses of androgen in a few reported instances seem to have been helpful in causing local tumor regression while awaiting the natural menopausal changes.

CASE REPORT

Mrs. M. L., aged 30 years, first consulted Dr. J. P. Greenhill on June 25, 1936. She had been married for 5 years and had never been pregnant. In 1926 she had had a laparotomy at which time both fallopian tubes and the appendix were removed. Seven years later in 1933 patient stated that a cystic right ovary was removed and the entire uterus was excised at that time. The patient's chief complaint at the time of the first visit in 1936 was a constant burning pain in the right lower abdomen and pelvis, frequent hot flashes, and vague bladder trouble. This bladder distress had been present according to

the patient for the last 7 years without relief. At first the symptoms were mainly those of pain on urination with a clock-like frequency day and night every 3 to 4 hours. Cystoscopic examination had been done in 1930 by a urologist who told the patient she had ulcers of the bladder wall. These had apparently been coagulated by cystoscopic fulguration. The patient had not menstruated since hysterectomy in 1913, but symptoms of the catamenia were present, particularly cramps in the lower abdomen every month and tenderness of the breasts for a week before the abdominal cramps appeared.

The physical examination showed a rather thin patient weighing 110 pounds. Breasts were normal. There was a linear, healed, abdominal scar which was well healed. The bimanual examination revealed a definite fulguration of the vaginal vault. All that remained of the cervix was a small tag of tissue. In the midline of the vaginal vault was a small, hard, tender mass about 1 centimeter in diameter which felt like a small uterus. The rest of this was an exquisitely tender round, cystic mass about 4 centimeters in diameter. Rectal examination corroborated these findings. A diagnosis was made of left ovarian cyst and laparotomy was advised. However, in view of the fact that the patient already had had two laparotomies, it was decided to treat her conservatively by means of the Elliott heat therapy for the pelvic pain and estrogens for the hot flashes. This therapy was carried out intermittently for more than a year during which time the patient gained weight and felt much better. The abdominal and pelvic discomfort decreased in severity and the hot flashes were considerably reduced. On September 2, 1937, the patient complained of itching in the vaginal region following urination. There was also considerable pain accompanying the act of voiding. Vaginal examination revealed the same findings as on June 25, 1936. Catheterized specimen of urine contained pus, blood, and bacteria. The patient was referred to a urologist who performed a cystoscopic examination and stated that he found nothing wrong with the bladder. Urine findings returned to normal after taking large quantities of fluid and urinary antiseptics.

The patient was not seen again until March 4, 1940. During this interval she had given herself hypodermic injections of estrogen to relieve her hot flashes. She was asked to stop this medication and to take diethylstilbestrol by mouth for 2 weeks at a time with intervals of 1 week's rest between.

On June 16, 1942, the patient returned complaining that she had had severe sharp pain in the lower left quadrant of the abdomen for the past week. Abdominal examination revealed considerable tenderness in both lower quadrants, especially marked on the left. Bimanual examination revealed a tender, fixed, small mass in the right side of the pelvis and a larger cystic, less tender mass on the left. Rectal examination confirmed these findings. The diagnosis made by Dr. Greenhill at this time was bilateral ovarian cysts in spite of the history of the removal of

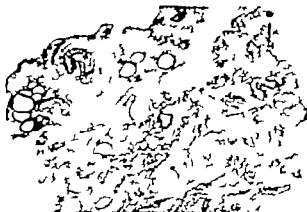


Fig. 2. Low power photomicrograph showing full thickness of bladder wall with extensive involvement of mucosa and submucosa forming an elevation. Distended glandular structures within the muscle layer resemble distended blood vessels in this low power photomicrograph. $\times 4$



Fig. 3. High power photomicrograph showing irregularity of glands, variation in height of lining epithelium and endometrial type of stroma about some of the glands. $\times 7$

the right ovary in 1933. Laparotomy was performed on August 26, 1942. The abdomen was opened, numerous adhesions were seen between the small and large intestines and the bladder, the cul-de-sac and the abdominal wall. All these were separated and both ovaries were found to be present. Both were converted into complete cystic masses. The right ovary contained typical old chocolate colored blood. The entire right ovary was removed and all of the cystic portion of the left ovary. A small piece of the left ovary was allowed to remain because of the patient's being only 36 years of age. (This obviously was an error particularly in view of the fact that the patient had had menopausal symptoms even when both ovaries were still present.) After the ovaries were removed exploration of the pelvis showed a hard round mass occupying the under portion of the bladder for a distance of 3 centimeters in the general diameter. This area was partially dissected out and was found to extend into the cavity of the bladder. The bladder was purposely opened and it was seen that there were numerous necrotic projections and cystic polyps on the posterior bladder wall. In view

of the negative findings on cystoscopic examination by two well known urologists a diagnosis of endometriosis of the bladder was not even considered by Dr. Greenhill. The bladder was closed with catgut and the line of suture covered with a piece of free omentum. A retention catheter was placed in the bladder after the abdomen was closed. Microscopic examination of the right and left ovarian tissues showed marked proliferation of endometrial glands. After recovery from this operative procedure the patient was again referred to another urologist, the third to beverly her. He stated, after cystoscopic examination, that the patient had "benign polyps" of the bladder and practiced fulguration through the cystoscope weekly for 3 months. The patient declined further treatment because the vesical symptoms were aggravated by this procedure.

On May 5, 1943, the patient consulted Dr. Greenhill complaining of constant pain in the right lower quadrant which radiated to the back and was accompanied by hot shooting pains into the rectum. There was no pain on urination and only an occasional hot flash. Vaginal examination revealed a very tender mass about 3 centimeters in diameter occupying the superior vaginal vault in the region of the posterior wall of the bladder. Dr. Greenhill considered this to be the mass which he found at operation to extend into the bladder. He referred the patient this time to Vincent J. O'Connor, the fourth urologist to observe the patient's bladder. Cystoscopic examination at this time showed a bladder to be normal in every respect except for the entire posterior wall which was occupied by a cystic mass about 4 centimeters in diameter. The cystic protrusions were very characteristic of so-called chocolate cysts of the ovary and presented an appearance which could be definitely diagnosed as an endometrioma of the bladder. Because of the extensive lesion and the fact that the patient had had persistent vesical symptoms for such a long period of time and because of the extent of the endometrial invasion of the bladder wall, it was felt advisable to resect this area completely. On May 24, 1943, the patient was operated upon by Dr. O'Connor at the Wesley Memorial Hospital. The bladder was mobilized extraperitoneally and no evidence of endometrial tissue projecting through the pelvic peritoneum could be found. An endometrioma about 1 centimeters in diameter was resected from the posterior bladder wall and an excellent closure of the bladder was possible. There was no evidence of obstruction to either ureteral orifice. Following this procedure Dr. Greenhill removed the remaining piece of ovary which was difficult to find in that it lay in the left upper pelvic region but seemed to be freely movable and had enlarged somewhat since the previous operation. Descriptions of the endome-

troma and the remaining piece of ovary are contained in Dr. E. R. Strauser's report which follows:

Gross description The portion of bladder wall removed at surgery measures 6 by 3 by 3 centimeters. On the external surface are numerous dark reddish brown nodular raised areas varying from less than a millimeter to 4 millimeters in diameter. On the cut surface of the tissue these nodules show as slightly raised pigmented areas scattered throughout the entire thickness of the bladder wall and even producing pigmented elevations on the mucosal surface. The involved portion of the bladder wall averages 3 centimeters in thickness.

Microscopic description The most striking histological feature is the presence of large angular or rounded glandular structures scattered through out the entire thickness of the bladder wall between the bundles of smooth muscle. Some of these glands are surrounded by the endometrial type of stroma but others are immediately bounded by the muscle bundles. Hemorrhage is present in the stroma about many of these glands. The epithelium lining the angular glands varies from low to high columnar type and in places is ciliated. Cellular outline is not very distinct but can be recognized in these glands. In the rounded or oval glands which appear to be distended by secretion the epithelium is much lower and the cellular outlines are almost completely obscured. In some of these glands the nuclei appear to be in a syncytium with the axes of the nuclei parallel to the basement membrane. The lumens of the distended glands contain grayish blue material (hematoxylin and eosin stain) or hemorrhage in most cases. The glands are most numerous on the mucosal side of the bladder wall but none can be seen to extend to the mucosal surface. The mucosal epithelium is almost completely destroyed and both mucosa and submucosa are markedly injected and moderately hemorrhagic. Congestion and edema are general throughout the bladder wall. Inflammatory infiltration consists almost entirely of lymphocytes and plasma cells mostly in the superficial portion of mucosa along the surfaces denuded of epithelium.

Diagnosis Endometrioma of bladder wall

The patient made an uneventful recovery and left the hospital on the twelfth postoperative day.

Pelvic examination on July 1, 1944 showed a vaginal vault free of masses and tenderness. Cystoscopic examination on July 15, 1944 showed a bladder capacity of 14 ounces. The bladder was normal in every respect. The patient states that for the first time in 10 years she can sleep 7 to 8 hours without voiding. The patient is in excellent health except that she continues to take an occasional course of diethylstilbestrol to control the hot flashes.

ENDOMETRIOSIS OF THE URETER¹

A careful review of all the available literature has revealed only one previously reported



Fig. 4. Bilateral pyelograms. Normal right pyelonephrogram, left, with filling defect in lower left ureter due to an endometrioma.

instance of intraureteral endometrioma. This patient was operated upon by Randall in 1940 and was reported at the meeting of the American Association of Genito-Urinary Surgeons in 1941. Randall states: "I fear that from symptomatology and from roentgenographic visualization such growths have heretofore masqueraded as primary ureteral neoplasms. And this case may report a great surgical rarity, but it is more likely that we have overlooked the diagnosis in some of our cases."

CASE REPORT

Mrs. E. S., a widow aged 50 years, entered the Lake Forest Hospital under Dr. Theodore Proxmire on March 26, 1944. Her chief complaint was left lumbar pain, chills and fever, recurrent hematuria and pyuria for the preceding 3 weeks, intermittent dysuria with marked frequency and urgency, had been present for 2 weeks. On admission to the hospital the patient felt quite ill, had a temperature of 100 degrees, pulse 100, respiration 20, marked pain and tenderness in the left costovertebral region.

¹are indebted to Drs. Theodore Proxmire and Donald B. Douglas of Lake Forest (Ill.) Hospital for permission to report this unusual case.



Fig. 5. Low power photomicrograph of the ureter wall showing splitting of the muscle layers by the endometrial tumor. A part of the glands are distended with blood and thrombus debris. Note marked flattening of the epithelium and a few distended glands show slight hyperplasia. $\times 33$

Blood examination showed 9,000 leucocytes, 70 per cent hemoglobin, 450,000 red cells. The urine contained 4+ albumin, much blood and pus, many bacteria (colon bacilli on culture).

The patient's history was unimportant except that she had had a vaginal hysterectomy in 1934. One daughter, aged 24 years, is living and well.

The general physical examination was negative except for the left renal tenderness with radiation of pain to the left groin. Sulfadiazine therapy was employed without improvement. Dr. Donald B. Douglas was then called in consultation by Dr. Proxmire. On March 29, 1944, vaginal examination showed no palpable masses or other pelvic abnormality. Cystoscopic examination was done under spinal anesthesia by Dr. Douglas who noted no urethral obstruction, moderate hyperemia of the bladder floor and trigone, mild trabeculation of the bladder wall, normal ureteral orifices. The bladder urine was diffusely cloudy, contained much pus and blood, and colon bacilli were found in culture. Both ureters were catheterized 30 centimeters. The urine from the right kidney was clear and uninfected. The urine from the left kidney was cloudy, contained 20 to 25 pus cells per high power field, 12 to 20 red blood cells, a rare cast. Scout x-ray films showed no shadows suggesting urinary calculi, bony outlines were normal, normal renal contours. Right pyeloureterogram was normal in every respect. The left pyeloureterogram showed marked dilatation of left renal pelvis with blunting of the calices and dilatation of the ureter extending down to the level of the bifurcation of the iliac vessels. Excretion urograms were made on March 30, 1944, and showed a normal excretion and normal outlines in the right urinary tree, decreased concentration with repetition of the left side filling defects previously noted in the retrograde pyelograms. The patient's condition showed no

lasting improvement on palliative treatment, and Dr. Douglas advised that a left nephrectomy be performed. The patient suggested consultation and Dr. O'Connor also was requested to review the case.

On April 7, 1944, the patient was running an intermittent fever up to 103.2 degrees, pulse 110, and was complaining of severe pain in the left loin. At the time of this consultation the only physical finding of note was a persistence of the left costovertebral tenderness on deep palpation. Neither kidney was palpable. A review of the previous urograms at this time suggested a filling defect in the lower left ureter. Dr. Douglas verified the persistence of this defect the following day by repeating the retrograde injection of the left ureter with opaque material. In view of these findings all concerned agreed on a diagnosis of a probable primary tumor of the left ureter, left hydroureter, and infected hydronephrosis. On April 10, 1944, a complete left nephroureterectomy was performed by Drs. Douglas and Proxmire. The left ureter was seen to be dilated down to the brim of the bony pelvis at which point it seemed very adherent to the posterior peritoneum. The peritoneum was opened and a somewhat enlarged but otherwise normal appearing left ovary was seen. After closure of the peritoneum the ureter was severed at the bladder level and the kidney and ureter were removed intact in the usual manner. Separate incisions in the lower abdomen and lumbar regions were made. The patient made a satisfactory convalescence and was discharged from the hospital May 8, 1944, relieved of all symptoms.

Pathologic report by Dr. Henry Halley: These left kidney and ureter

Gross: Kidney slightly smaller than average, is changed by a moderate degree of dilatation of the calices and pelvis with atrophy of pyramids and slight atrophy of the cortex. The markings of which are still distinct. The kidney is 11 centimeters in length and weighs 5 grams without its capsule.



Fig. 6. High power photomicrograph of the ureteral wall showing slightly hyperplastic gland in which the basal epithelium is greatly increased in height. Other less hyperplastic glands have lower epithelium. $\times 63$.

The obstruction is in the ureter at a point about 14 centimeters below the ureteropelvic junction in the fixed specimen due to a thickening of the wall of the ureter by a poorly circumscribed nodule which diffusely extends in the wall extending into the lumen in the form of a small polyp about 5 millimeters in diameter with a smooth covering. The ureter has been opened previously and the lumen is almost absent at this point, being normally patent below the polyp and dilated to a diameter of about 1 millimeter above it. Just above the obstruction the wall of the ureter is thick and the soft tissue is dark red as from congestion. The wall thickens toward the kidney and the lumen less dilated of greater size than normal. About 4 centimeters the ureter is attached below the obstruction. The ureter is in two pieces, one piece attached to the kidney 10 centimeters in length.

Histology. The obstructed part of the ureter is divided into four pieces. Examination of these shows an overgrowth of glandular tissue surrounded by an overgrowth of stroma which is cellular and fibrous. This tissue most nearly resembles transitional tissue. This is evidenced by the formation of glands which vary in size from small to medium and are lined chiefly with columnar epithelium. In some places basophilic cells like the peg cells of the transitional epithelium.

The overgrowth is largely without the muscle, mostly in and outside the wall extending into the muscle and forming a flattened plaque above the outside corresponding to the thickened wall above the polyp. The polyp itself is a protrusion of the glandular overgrowth into the lumen of the ureter and is covered with transitional epithelium like that of the ureter. The lumen of the ureter is lined with typical transitional epithelium differing from that of the overgrowth and the lumen is

pushed to one side where the tumor pushes into the ureter. In sections taken from the obstruction a few remnants of the endometrial tissue are observed in the connective tissue about the ureter.

In several sections of the kidney there are slight changes in the pyramids and cortex chiefly dilatation of the tubules in the pyramids and disseminated renal atrophy in the cortex perpendicular to the vasa recta with beginning fibrosis of the stroma and dilatation of the corpuscles. Changes in the tubules are minimal. There is no significant acute inflammation of the tubules. These changes are in keeping with chronic nephrosis.

Endometrosis of the ureter with chronic nephrotic atrophy of the kidney.

Summary

The case of the subject of endometrosis of the bladder and ureter suggests that these cases are probably rare and more common than the literature indicates. This report is intended not to add additional instances of vesical endometrosis but to emphasize the importance of recognizing this condition in the differential consideration of tumors of the bladder and ureter.

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RAPID REPAIR OF DEFECT OF FEMUR BY MASSIVE BONE GRAFTS AFTER RESECTION FOR TUMORS

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THE present is an appropriate time for consideration of the repair of defects in the large long bones in view of their increased frequency occasioned by the war and by a greater tendency toward resection of carefully selected cases of bone tumors, particularly slowly growing sarcomas and borderline cases that are recognized early and are favorably located for resection. Two cases of tumors falling in these classes are reported because they show the rapidity with which a missing segment of the femur may be restored by the use of massive bone transplants permitting much earlier resumption of function than has been usual in the cases heretofore reported.

The essential steps of the operation were as follows: under a tourniquet, resection of the involved region and removal of two tibial grafts each between two-fifths and one-half the circumference of the shaft; completion of hemostasis after removal of tourniquet; insertion of the grafts in part onlay and in part intramedullary and fixation to the fragment at either end with two large threaded wires, thereby replacing the missing segment by bone averaging 85 to 90 per cent of the size of a segment of tibia; cast fixation until the completion of bony union followed by walking caliper splint support during the major portion of the period of hypertrophy and transformation of the grafts.

CASE 1: Male aged 26 years, had had pain in the left knee for 6 months before admission which had greatly increased in severity in the previous 3 months and was associated with slight swelling, limitation of motion and a limp. Otherwise he had been in his usual good health and there had been no change in weight. Previous and family histories irrelevant. Physical examination revealed a healthy appearing man of stated age with essentially normal findings aside from the left lower extremity. Motion in the knee was limited 50 per cent and there was a small swelling of the medial condyle which on

palpation was firm and slightly sensitive. Urine and blood findings, including serology, were normal.

Röntgenograms of the knee (Fig. 1) revealed a circumscribed region of reduced density involving the entire medial condyle, the intercondylar region, the mesial margin of the lateral condyle and the mesial portion of the distal $\frac{3}{4}$ inches of the shaft. In the anteroposterior view there was visible a faint triangular shadow of increased density along the surface of the mesial cortex above the region of reduced density and below this a faint shadow of bony density bulging peripherally suggesting an outward bending of eroded cortex by tumor which had completely destroyed and broken through the bone below. Röntgenograms of the chest revealed no abnormal findings. The diagnosis was made of tumor, either a benign or because of the layer of periosteal new bone above and the break through of overlying cortex a malignant giant cell tumor. It was decided that if on biopsy the lesion were found to be benign it would be treated by curettage and transplantation of bone into the cavity, but if malignant, the treatment would be by resection of lower end of the femur, overlying quadriceps muscle, knee joint and upper end of epiphysis of tibia and bone transplantation.

Operation: The entire left lower limb and hip were prepared by skin sterilization with iodine and draping with sterile sheets. A sterile Martin bandage was applied spirally from the foot to the upper thigh. In order to have the hip construct completely out of the field of operation a Steinmann pin was then passed through the muscles above the greater trochanter and a sterile 1 inch rubber tube was passed twice around the hip above the pin, and tied. From the biopsy through an anteromedial incision and frozen section it was concluded that the tumor was a malignant giant cell tumor. The biopsy incision was closed and an elliptical incision made about 1½ inches above the knee and extending over the upper 3 inches of the tibia anteriorly. The skin flaps were reflected laterally and medially exposing the quadriceps muscle which was divided about 4 inches above the joint line and freed from the posterior muscles, long to mesial and lateral borders. All detectable blood vessels were clamped, divided and ligated as the operation proceeded. The quadriceps muscle was severed 4 inches above the line of the knee joint and the femur was then divided at the same level with wire saw. Next the lower fragment was brought forward and separated from above downward from the undivided hamstring muscles and origins of the calf muscles, the superior knee vessels being divided and ligated.

From the Department of Surgery, The University of Chicago.



Fig. 1

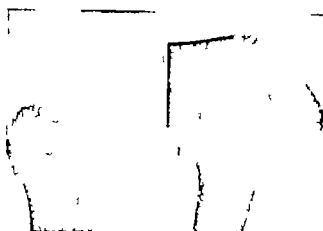


Fig. 2



Fig. 3

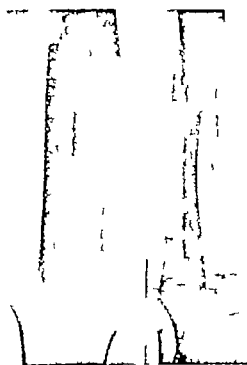


Fig. 4

Fig. 1. Case 1. Destructive lesion of medial femoral condyle with triangle of periosteal new bone above.

Fig. 2. Case 1. Roentgenogram of excised specimen.

Fig. 3. Case 1. Three months after operation.

Fig. 4. Case 1. Five and one third months after operation.

near their points of origin from the popliteal artery and vein. The reflection was carried downward just beyond the limits of the joint capsule; the tibioapatellar tendon divided and the upper 3 inch of the tibia sawn off removing the knee joint intact. Figure 2 shows a roentgenogram of the specimen which measured 4 3/4 inches long. The skin incision was then extended downward over the front of the tibia to its lower end. With a motor saw a bone graft including periosteum was cut from the shaft, 1 1/2 inches long and encompassing two-fifths of the circumference of the cortex above and increasing to one half at the lower end. It was then divided at the middle. The proximal half was reversed and its ends

were inserted into the medullary cavity of the tibia and femur in the coronal plane. The distal half was reversed and applied in the sagittal plane into the medullary cavity of tibia and laid on cortex of femur. Fixation was by two threaded heavy wires passed through both grafts and the shaft at either end.

The two grafts were in contact with each other below and cancellous bone from the sagittal graft bridged most of the intervening space above. What space was left was bridged with small cancellous grafts. The wound was closed without drainage and a body and left lower limb plaster cast was applied. Because of the use of the tourniquet and careful hemostasis there was very little blood lost and con-



Fig. 5

Fig. 6



Fig. 7

Fig. 8

- Fig. 5. Case. Ten months after operation and 1 month after fracture medial graft.
 Fig. 6. Case. One year after operation. Fracture healed.
 Fig. 7. Case. Two years and 5 weeks after operation. Fresh fracture in medial graft.
 Fig. 8. Case. Three and one-third years after operation.

sequently no shock. Convalescence for the next 7 weeks was uneventful at the end of which time the cast was removed and bony union between grafts and fragments was present (Fig. 3).

The limb was then placed in a walking splint, and at the end of 4 months the patient returned to fitting work as a linotype operator which has now been continued for 3½ years without inter-



Fig 9. Case 1. Tumor spreading from neck of femur and triangle of periosteal new bone above.

tion because of the leg. At the end of 5 months the wires were removed under local anesthesia. Roentgenograms 2 weeks later (Fig 4) showed evidences of firmer fusion of grafts and trabecular bridge between the lower halves of the grafts. A layer of new bone along the surface of the shaft of the lateral graft. The tibial defect left by removal of the graft showed signs of advanced repair.

The patient returned 10 months after operation, stating that he had been working steadily since removal of the brace but that during the past month he had had pain in the lower part of the left thigh on walking which had occasioned very little inconvenience.

Roentgenograms (Fig 5) revealed still more fusion of grafts and shafts and slightly mottled shadow in the lower portion of both grafts and the upper portion of the lateral one, the result of replacement of the dead cortex by new bone. There was an oblique line of reduced density extending across the lower third of the mesial graft with a shadow of increased density about the surface indicative of a healing fracture. He was allowed to continue walking and working and the pain soon disappeared. A roentgenogram (Fig 6) 1 year after operation revealed a large dense shadow of bone bridging the fracture site. Sixteen months after operation the splint was discarded and he walked without support until 2 years and 5 weeks after operation when he returned stating that for 3 days he had again had pain in the lower part of the thigh. Roentgenograms (Fig 7) revealed further mottling of density of the grafts as evidence of creeping replacement of the dead cortex by living bone. There was an oblique fracture line in the anterior portion above the middle of the mesial graft seen in the lateral view.

He continued work, wearing the brace except at night for 4 months, at the end of which time roentgenograms revealed healing of the fracture with a large spindle-shaped bony callus. The brace was discarded, and he has since been active on the limb without difficulty. His general health has remained excellent and at the time of writing 3 years and 6 months after operation he was free from signs of recurrence of the tumor as determined by general physical examination and roentgenograms of the

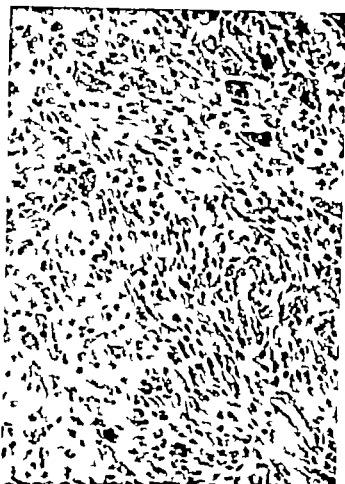


Fig 10. Case 1. Photomicrograph, X195 at junction of giant and spindle cell regions.

chest and of the operation site (Fig 8). The callus is much more dense and spindle-shaped at the site of the upper fracture than of the lower one in the mesial graft. The two grafts are fused except for a short narrow window near the upper end and there has been considerable hypertrophy and transformation in the direction of a tubular bone as best indicated by a dense shadow of cortex laterally and rarefaction and marrow cavity formation centrally. Judging from the extent to which new lines have formed throughout the graft the dead bone has probably all been replaced by new bone. The tibial shaft while strong still shows some blotchy irregularity at the site of removal of the graft.

Gross pathology. On removal of the overlying soft parts and the attached portion of tibia from the femur the latter was found to contain a tumor bulging from the mesial and anteromesial sides of the interval condyle and end of the shaft. On coronal section a mottled grayish to brown globular mass of soft tissue replaces the bone of the mesial condyle in adjacent portions of the lateral condyle and end of the shaft (Fig 9). There was a triangular layer of spongy new bone extending upward 1½ inches beneath the periosteum of the shaft. The articular cartilage and the synovia overlying the tumor anteriorly were not invaded.



Fig. 1

Fig. 1. Case 1. Central destructive tumor with marked round growing bone formation.



Fig. 2

Fig. 2. Seven days after operation.

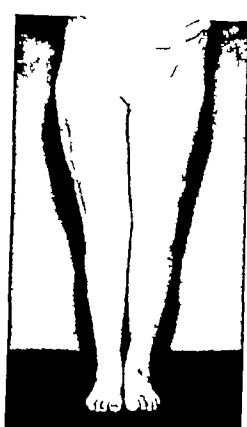


Fig. 3

Fig. 3. Case 2. Photograph showing appearance of limbs 13 years and 6 weeks after operation had been carried out.

Microscopic pathologic. A microscopic section was cut of the lower 3 inches of the femur traversing the entire lesion. A broad zone of the deepest portion of the tumor and extending into the lateral condyle consisted of large numbers of multinuclear giant cells of the foreign body type intermixed with mononuclear polyhedral and spindle cell typical of a benign giant cell tumor. Proceeding medially to the surface of the tumor the incidence of giant cells decreased with replacement by nests and bands of round and polygonal cells which resembled sarcoma although mitotic figures were absent and hyperchromatic nuclei were rare (Fig. 1). It was a frozen section of this type of tissue which led to the initial diagnosis of sarcoma. The triangular area along the cortex also, though it consisted of new nontumorous bone, similar to that formed by the periosteum about the margin of a few giant sarcoma.

The most appropriate diagnosis in view of the microscopic appearance, the triangular layer of periosteal reactionary new bone and the freedom from metastases after 3 1/4 years is a borderline tumor between benign and

malignant giant cell tumor which justifies the operation which was carried out.

CASE 2. A female aged 11 years entered the clinic because of a progressive pain in the lower right thigh of 4 months duration. It was aggravated by walking and prolonged exertion caused a limp. Sixteen months previously she had an operation elsewhere for a lesion of the femur in that region which was found to be a centrally situated rich cellular cartilaginous tumor considered a benign but bordering on malignant. Patient and family histories irrelevant. Physical examination revealed a healthy appearing obese girl who presented no abnormal findings except in the right thigh. There was a 5 inch longitudinal incisional scar on the outside of the thigh extending down and from the middle and deep palpation at that level revealed a slight nontender elliptical swelling of the shaft of the femur. Blood and urine analyses revealed no abnormalities and the Kahn test was negative. Roentgenogram revealed a spindle shaped halo of increased density of the shaft of the right femur 6 inches long beginning 2 1/2 inches above the lower epiphysis. In the middle of the medullary region of the sclerosed



Fig. 14.

Fig. 15.

Fig. 14. Case 2 a, left Nineteen months and, b 3 years and 6 weeks after operation
Fig. 15. Case 2 Four years and 3 months after operation.

and enlarged segment, there was an oval area of reduced density $2\frac{3}{4}$ inches long (Fig. 11). Chest roentgenograms showed no abnormalities.

Because of the previous removal of a richly cellular cartilaginous tumor followed by recurrence and very marked thickening and sclerosis of the shaft about the central area of reduced density, the diagnosis of a slowly growing central chondrosarcoma appeared to be justified. A previous report from this clinic of chondrosarcoma of the femur has shown quite similar roentgenological findings in some of the cases in which the shaft of the bone is involved centrally. In view of the well known tendency recently reviewed by Gulecke of these central chondrosarcomas to grow more slowly and to metastasize later than most other sarcomas, it was decided to resect the involved segment and replace it by two heavy bone grafts taken from the tibiae. In view of the recurrence after the previous curettage resection would have been indicated had the lesion been benign.

Operation. Both lower limbs and the right pelvic region were prepared by iodine skin sterilization and draping with sterile sheets. A Martin rubber bandage was applied spirally to the right leg from toes to



Fig. 16. Case 2 Sections of the tumor longitudinally with cartilage filling the large central area and the three small areas, x



Fig. 1

Fig. 2

Fig. 1 Case 1 Central destructive tumor of the femur surrounded by new bone formation.
Fig. 2 Seven days and 8 months after operation.

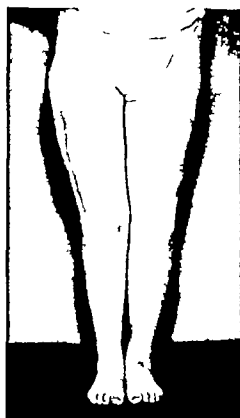


Fig. 3

Fig. 3 Case 2 Photograph showing appearance of limbs 3 years and 6 weeks after operation had been carried out.

Microscopic.—*Histology.* A macroscopic section was cut of the lower 3 inches of the femur traversing the entire lesion. A broad zone of the deepest portion of the tumor and extending into the lateral condyle consisted of large numbers of multinuclear giant cells of the foreign body type intermixed with mononuclear polyhedral and spindle cells typical of a benign giant cell tumor. Proceeding medially to the surface of the tumor the incidence of giant cells decreased with replacement by sheets and bands of round and spindle cells which resembled sarcoma. Although mitotic figures were absent and hyperchromatic nuclei were rare (Fig. 1) it was a frozen section of this type of tissue which led to the initial diagnosis of sarcoma. The triangular area along the cortex above the tumor consisted of new nontumor bone similar to that often formed by the periosteum about the margin of a living sarcoma.

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The most appropriate diagnosis in view of the microscopic appearance, the triangular layer of periosteal reactionary new bone and the freedom from metastases after 3½ years is a borderline tumor between benign and



Fig. 14.

Fig. 14. Case 2. a, left. b, sixteen months after operation. c, d, b, 13 years and 6 weeks after operation.

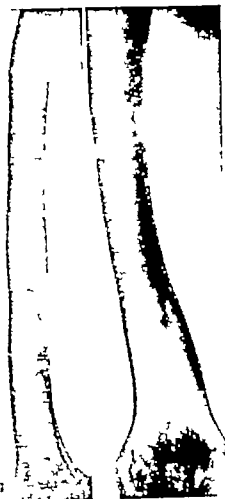


Fig. 15.

Fig. 15. Case 2. Four years and 3 months after operation.

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Because of the previous removal of a richly cellular cartilaginous tumor followed by recurrence and very marked thickening and sclerosis of the shaft about the central area of reduced density, the diagnosis of a slowly growing central chondrosarcoma appeared to be justified. A previous report from this clinic of chondrosarcoma of the femur has shown quite similar roentgenological findings in some of the cases in which the shaft of the bone is involved centrally. In view of the well known tendency, recently reviewed by Gulecke, of these central chondrosarcomas to grow more slowly and to metastasize later than most other sarcomas, it was decided to resect the involved segment and replace it by two heavy bone grafts taken from the tibiae. In view of the recurrence after the previous curettage, resection would have been indicated had the lesion been benign.

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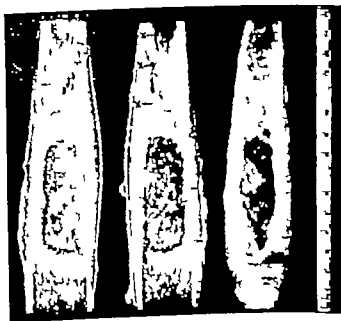


Fig. 16. Case 2. Sections of the tumor longitudinally with cartilage filling the large central area and the three small areas, x.

upper thigh, a Steinmann pin was introduced through the soft parts above the greater trochanter and a heavy 1 inch rubber tube tourniquet passed twice around the hip above it and tied. Through a 9 inch lateral incision the involved femur was exposed laterally cutting wide of muscle attachments and periosteum until the upper and lower limits of the enlargement had been reached. The bone was severed at the lower end with a wire saw, the upper fragment brought out of the wound and the soft parts at attachments divided wide of the bone posteriorly and mesially. Six inches of the shaft was then resected. The fragment ends above and below appeared to be free of involvement. To prevent the possibility of transplanting tumor the gloves and instruments were changed. Through a 9 inch incision a graft 7½ inches long and comprising slightly less than one half of the circumference of the right tibia was cut and the wound was sutured and temporarily bandaged. The hip tourniquet was then removed and bleeding points that had not been controlled were clamped and ligated. Gloves were again changed and a second graft similar to the first was taken from the left tibia under a tourniquet. One graft was inserted into the defect intramedullary in the coronal plane and the other onlaid in the sagittal plane. At either end two large threaded wires were inserted obliquely with the intention of perforating shaft and both grafts with each wire. Below where the cortex of fragment was thin they were easily inserted. But above where the cortex of fragment was thick and dense the wire wobbled and enlarged the holes in the onlay graft. Also the upper wire was inserted too high and missed the end of the intramedullary graft. (The oblique insertion engendered by fear of splitting the end of the onlay graft, was a mistake and in subsequent operations the wires have been introduced perpendicularly as in Case 1.) After closure of the wound without drainage a cast was applied to the body and both lower extremities. There was relatively little blood loss but as a safety measure the patient was given a 500 cubic centimeter blood transfusion during the operation. Shock did not develop and the early postoperative course was uneventful. A roentgenogram 7 days later showed the fragments and transplants to be well aligned (Fig. 15 left).

However another roentgenogram taken 3 months later revealed that the poor fixation by the wires at the upper end had permitted angulation within the cast and that bony union had occurred between the grafts and the fragments. Cast immobilization was continued for 5 months, and then a caliper splint was applied after which walking was gradually resumed. Figure 13 right shows the roentgen appearance 8 months after operation with fusion of the grafts and already considerable progress toward transformation into a tubular bone. The wires were then removed and walking without support was begun at 10 months. The grafts rapidly hypertrophied and transformed as shown by serial roentgenograms and at the end of the year she was fairly active with

about 90 degrees of motion at the knee, only a slight limp, and the legs equal in length. Figure 14, a and b shows roentgenograms 19 months and 13 months and 6 weeks respectively after operation, and Figure 13 is a photograph at the latter date. It is safe to assume from the roentgenographic appearance due by the 19th month absorption and replacement of the old dead bone was practically complete. Side and front views at the end of 4½ years are shown in Figure 15 at which time roentgenograms of the chest were negative. At the time of reporting 4½ years after operation the limbs were of equal length, and the knee could be flexed to 120 degrees. There is still a very slight limp due to the bowing of the shaft and some degree of external rotation of the upper fragment.

Pathological report. After trimming off the attached muscle fragments the spindle-shaped segment of shaft was covered by an adherent periosteum and the window made by the previous operation was closed by new bone. Section of the shaft longitudinally revealed the oval central area filled with soft, dark bluish-gray cartilage (Fig. 16). The surrounding cortex was expanded and thickened and the medullary cavity was filled with dense new bone below for a distance of ¾ inch and above for 2 inches. Three small islands of cartilage were seen in the upper end of the sclerotic bone of the medulla at the points marked x.

A microscopic section was made of the slice cut out of the middle of the entire specimen. The tissue filling the central cavity as well as the three islands above was composed of immature hyaline cartilage which was richly cellular and was growing cauliflower-like about the periphery. There was evidence of surface erosion and slight superficial invasion of the surrounding bone by the tumor. The new bone filling the medullary cavity above and below consisted of dense trabeculae with fibrous and hematopoietic marrow. The cortical thickening was due to deposition of coarsely lamellated reactionary new bone mainly subperiosteally and to a lesser extent endosteally. The diagnosis was central chondrosarcoma of low grade malignancy with reparative new bone filling out a defect in the upper portion which had been left after the previous operation.

While healing in these 2 cases was by primary intention experience with other cases (3) has shown that the incidence of infection in the transplantation of massive bone grafts for the repair of large defects following excision of bone tumors is higher than for the average run of large clean operation. Also in case of large defects of bones created by injury which are usually infected and by extensive osteomyelitis with death of a large amount of shaft, the risk of infection following massive transplantation is so great that an operation in which

this technique is used should not be performed until all wounds have been healed for at least 2 years

Metal screws may equally well be used for fixation of the graft and do not have to be removed but threaded heavy wires are more quickly and conveniently inserted as no preliminary drilling is necessary. They may also be cut close to the bone and left permanently

SUMMARY AND CONCLUSIONS

Two tibial grafts which together equalled approximately $\frac{3}{4}$ the size of the missing segment of bone were anchored to the fragment ends by threaded wires to bridge a defect of the femur in 2 cases after excision for bone tumors. Bony union occurred between the fragments and grafts almost as rapidly as it occurs between fragments in the healing of a simple fracture. The large bridge supported the limb so well that with the aid of a caliper splint walking was resumed in 4 months in 1 case and in 5 months in the other. A series of roentgenograms taken at intervals following operation revealed that in each case after the completion of bony union and the resumption of function of the extremity there was gradual hypertrophy of the grafts absorption and replacement of their cortical bone by new bone and transformation of the bridge into a segment of tubular bone resembling the missing part. In Case 2 occurring in a young adolescent the progress was relatively rapid and the transformation was almost as marked at the end of 2 years as at the last x ray examination $4\frac{1}{2}$ years after operation when a very good replica of the original bone was seen.

In Case 1 occurring in a 28 year old man the transformation was much slower and brace support was necessary for a longer period. Also because of insufficient hypertrophy pre-

vious to the period of creeping replacement of the old dead bone by new bone (which at first is always weaker than the old bone) the mesial tract fractured twice first 9 months and second 5 months after operation. Each fracture healed while use of the limb was continued which stimulated a great deal of new bone formation and apparently hastened the process of creeping replacement of the graft. The last roentgenological examination $3\frac{3}{4}$ years after operation showed that the bridge had hypertrophied to a size that was adequate for full support of the limb and that creeping replacement of the old bone by new bone was apparently complete. However the transformation into a segment of tubular bone was still imperfect. And judging by the slowness of the change in this case during the last year and in other reported cases in adults after the lapse of 2 to 3 years it is anticipated that the shape will remain much as is shown in the last roentgenograms.

Because of the use of the tourniquet and of careful clamping and ligating of vessels the blood loss was slight and there was no shock despite the fact that the operations were very extensive and the amount of tissue devitalized in the transplants was great. All of which argues in favor of blood loss and against toxins and nociceptive nerve impulses as the cause of shock from such operations.

The freedom from evidences of local recurrence and of metastases after 3 years and 10 months in Case 1 and $4\frac{1}{2}$ years in Case 2 favors the use of the operation in carefully selected cases of slowly growing and borderline malignant tumors.

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responded with decrease to 20 units following castration. When it became apparent that he developed into a delayed failure there was only a comparatively slight tendency to increase in serum acid phosphatase activity which did not exceed 45 units shortly before death.

EFFECT OF TREATMENT ON METASTATIC LESIONS

Bone metastases Skeletal metastases were demonstrable in 59 patients. In 6 of them metastases became apparent during the course of treatment which indicates that androgen control treatment of prostatic cancer does not protect the patient from the possibility of metastatic spread of the disease.

Eleven of the 59 patients with metastatic bone lesions were excluded from this consideration because they either died less than 3 months after the start of treatment (9 cases) or they did not report for re-examination (2 cases).

In the remaining 48 patients the effect of treatment on the bone metastases proper was unsatisfactory as a rule. No noticeable changes in the appearance of the bone lesions in the x ray picture were observed in 13 cases. Further progression of previously demonstrable metastases or metastatic spread to other parts of the skeleton occurred in 25 patients. Six other patients, mentioned before developed bony metastases in spite of treatment.

Improvement in the roentgenological appearance of metastatic bone lesions was demonstrable in only 4 patients, but improvement was not sustained in 2 cases. Both of these patients developed into delayed failures 1½ years after beginning of treatment and died of the disease with widespread metastases. Improvement was sustained in the other 2 patients for more than 2 years, and both patients have remained in apparently good health up to the time of writing. In none of these patients have we been able to observe complete disappearance of bone metastases although improvement was remarkable in both instances.

Lymph node metastases Metastatic lymph node involvement was encountered in 6 pa-

tients and the diagnosis was confirmed by biopsy in each case. One of these patients had bone metastases in addition to lymph node metastases. All of these patients had metastases at the time of admission, and so far we have not observed any patients who developed lymph node metastases after being subjected to androgen control treatment.

In contrast to the poor results accomplished in the group of patients with bony metastases, the results obtained in patients with lymph node metastases have been satisfactory. Treatment was ineffective in only 1 patient who was admitted with general carcinomatosis in the terminal stage of the disease. Complete regression of the metastatic lymph nodes took place in the other 5 cases. None of them has developed recurrence, although 2 of them have been under treatment for more than 2 years. It is of interest that the patient who had metastases to bones and lymph nodes responded with regression of the metastatic lymph nodes while serial x-ray pictures revealed further progression of the metastatic bone lesions.

The degree of response to androgen control treatment was particularly impressive in the group of patients with lymph node metastases, and it seems that the favorable results accomplished are usually more sustained than the results accomplished in patients with metastatic bone involvement.

Lung metastases Metastases to both lung were found in 1 patient who died within 3 months in spite of treatment.

EFFECT OF TREATMENT ON SERUM ACID PHOSPHATASE

It is well known that patients with increased serum acid phosphatase activity due to bone metastases from prostatic cancer usually respond with decrease of the acid phosphatase following androgen control treatment. According to our previous experiences the mean decline of serum acid phosphatase in this group of cases amounted to 75 per cent of the original values 1 week after the start of treatment. Thereafter a less precipitous fall continued for 2 to 3 months until equilibrium was reached at a level of 93 per cent of the previous findings.

Our studies on this subject have been continued and similar initial results were obtained however during the course of investigations over a longer period of time we have been able to collect additional data which are of interest

Of the 65 patients with metastatic disease consistently normal values for serum acid phosphatase activity were determined in 13 cases (metastases to lymph nodes, 5 lungs, 1 bones, 7) In the remaining 52 patients all of them with metastatic bone involvement increased serum acid phosphatase activity was determined repeatedly It ensues that the acid phosphatase test was positive in 88 per cent of the 59 cases with bone metastases.

Marked decrease in serum acid phosphatase activity as a result of treatment developed in 36 patients. In 7 of these cases subsequent re-elevation of the serum acid phosphatase took place while in the remaining 29 cases improvement has been sustained up to the time of writing

No significant changes in the serum acid phosphatase level were noticeable in 6 patients and tendency to further increase in spite of treatment was determined in 7 patients.

The 3 remaining cases had consistently normal values for serum acid phosphatase in spite of the presence of metastatic bone lesions before and during the first 12 months of treatment however gradual elevation to values of between 10 and 15 King Armstrong units developed during the further course of observation.

Our studies dealing with changes in serum acid phosphatase activity following androgen control treatment of patients with bony metastases indicate the following conclusions

- 1 Determination of serum acid phosphatase is of only limited diagnostic value in patients who were subjected to castration or estrogen administration
- 2 Increase of serum acid phosphatase or consistently high acid phosphatase values, in spite of androgen control treatment should be interpreted as an unfavorable prognostic sign, indicating no or poor response to treatment

3 Delayed failures may develop although decrease of the serum acid phosphatase activity to persistently normal values has taken place Of 23 patients developing into delayed failures only 10 revealed a moderate tendency of the acid phosphatase to re-elevation while the 13 other patients maintained low acid phosphatase levels up to the terminal stages of the disease

ANALYSIS OF STUDY

Our studies on the effect of androgen control treatment of prostatic cancer have indicated that favorable response to this method of treatment was accomplished in numerous instances However during the course of prolonged observation it became evident that a considerable number of the group of patients showing initial improvement developed into delayed failures. The increasing frequency of such delayed failures as time progressed suggests that improvement in the remaining patients may not be sustained either Thus the conclusion presents itself that even the most spectacular improvement in any patient has to be viewed with skepticism as to the ultimate outcome

In the treatment of patients with far advanced or metastatic disease androgen control treatment has proved its value as a method to prolong life The degree of response to this method of treatment is much more impressive as a rule than the poor results accomplished by external or interstitial irradiation Although improvement is of temporary duration only the simplicity of the method and the low surgical risk involved justify its use in combination with the usual methods in the treatment of high grade urinary obstruction

Study of our material indicates that the results obtained were most favorable in the group of patients with metastatic lymph node involvement All but one of our patients with such lesions responded with complete regression of the metastases and so far none of them has developed recurrences. However the period of observation as well as the number of patients with lymph node metastases is insufficient as yet to allow definite conclusions.

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In contrast it has been our experience that spread or local extension of bone metastases

is not arrested as a rule by androgen control treatment. We also have seen patients with previously nonmetastatic disease who developed metastatic bone lesions, although they were under androgen control treatment for a considerable length of time. It ensues that this method of treatment does not protect the patient with nonmetastatic cancer of the prostate from developing metastases at a future time (Nesbit and Cummings).

In spite of the apparent ineffectiveness of androgen control therapy on the bone metastases proper it cannot be denied that many of these patients derive temporary benefit from this method of treatment such as disappearance or improvement of pain, gain in weight and increase in well being. Also improvement of obstructive symptoms and regression of the local lesion may take place until re-surgent symptoms usually indicating the terminal stages of the disease make it evident that the tumor has not lost its activity.

It is difficult to determine the value of androgen control treatment in patients with inoperable nonmetastatic prostatic carcinoma. It is well known that many of these cases may live comfortably for years without receiving any treatment. Although improvement of the primary lesion as a result of castration or stilbestrol administration develops in numerous cases, it remains doubtful whether or not the course of the disease is being influenced to an appreciable degree. The occurrence of metastases following years of androgen control treatment demonstrates that this method of therapy does not constitute a prophylaxis against development of metastatic lesions. We are in agreement with Nesbit and Cummings who express the opinion that the maximum benefit to the patient may be derived by delaying endocrine therapy until indicated by the onset of symptoms arising from advanced or metastatic lesions.

It is obvious from these considerations that androgen control treatment should be employed in accordance with certain indications and particularly orchidectomy should not be carried out indiscriminately in all cases of carcinoma of the prostate. Castration should be reserved for patients with metastatic

disease patients in whom metastases are suspected, or patients in whom rapid enlargement of the primary lesion becomes apparent. It is our impression that castration is the more effective procedure if quick relief from pain is the object of therapy. Combined treatment consisting in orchidectomy preceded or followed by estrogen administration does not seem to offer any advantage over castration alone. A comparison of the end results in the group of castrated patients with the end results in the group of castrated patients who received additional estrogen showed no appreciable difference. It is of interest in this connection that stilbestrol medication even in doses of up to 3 milligrams daily had no effect in 7 of 8 patients who developed re-surgent symptoms following orchidectomy. Only 1 of these patients responded with temporary improvement of 6 weeks duration.

Exclusive stilbestrol medication should have its place in selected cases of prostatic cancer. An indication for exclusive estrogen treatment is present in our opinion (1) in patients with operable carcinoma of the prostate who refuse surgery (2) in patients who refuse orchidectomy and (3) in patients with moderately advanced lesions of apparently low grade malignancy who have little or no symptoms. However castration should be carried out in the first or in the latter group of these cases if changes occur which indicate progression of the disease. We have castrated 19 patients in whom sudden progression of the disease became evident after they had received estrogen for a considerable length of time. Fifteen of them responded favorably although improvement was of only temporary duration in 5 of these cases. The 4 remaining patients showed no response.

This indicates that failures which occur following exclusive stilbestrol administration may be improved, at least temporarily by orchidectomy while estrogen administered in cases of failures following castration is ineffective as a rule.

It has been suggested by Huggins that castration or estrogen administration results in a reduction in the quantity and activity of circulating androgens, thereby causing decrease in size and function of the cancer cells.

He also believes that immediate or delayed failures of androgen control therapy are due to the presence of extragonadal foci of androgen production notably in the adrenal cortex. This theory finds support in an autopsy report by Herbst, who found enlargement of the adrenals to four and seven times the normal size in one patient with prostatic cancer who did not respond to castration. It must be kept in mind however that in addition to the adrenals the pituitary plays an important part in androgen control. It may be possible that the pituitary is the gland from which the stimulus originates which in time causes increased activity of the adrenals.

With this idea in mind we have given external irradiation to the pituitary in 23 patients. Two hundred kilovolts x radiation (half value layer 0.9 mm copper 50 cm skin target distance) was employed and the pituitary was irradiated from two lateral and one anterior portal delivering a total of from 1000 to 1,000 roentgens into the region of the sella turcica. The results accomplished were interesting but not conclusive. In reporting them it should be stressed that we do not claim spectacular results but our observations, which are based on experiences gathered for more than 1 year may stimulate continuation of these investigations.

One of these 23 patients was not included in our series of 130 patients because he did not receive androgen control treatment at any time.

II J aged 67 years white (Case No. 4877) was admitted to our service on April 30 1943. At this time he was unable to walk on account of severe pain in both hip joints and both legs which had persisted for 8 months. Biopsy from the prostate revealed carcinoma and x-ray studies showed bony metastases involving the lumbar spine pelvic girdle and both femurs. He received 200 kilovolts x radiation as indicated before and from May 5 to May 18 1943 a total of 1305 roentgens was delivered into the region of the pituitary. Improvement of pain occurred 3 days after beginning of irradiation and continued to such a degree that he was able to walk without any discomfort when he was discharged on May 24 1943. He continued to feel well when last examined on July 26 1943 however there was neither gain in weight nor increase in the red blood count nor decrease in the serum acid phosphatase activity or improvement of the primary lesion. One month later in August

1943 we were informed by his family physician that he had developed resurgent symptoms and that he was failing rapidly. He died of the disease on February 22 1944 at his home town and no autopsy was obtained.

The other 22 patients who received irradiation treatment over the pituitary were patients who developed into delayed failures following androgen control treatment. All of them were included in our series of 130 patients.

Twelve of these 22 patients did not respond to irradiation and continued to fail until they died of the disease. The other 10 showed varying degrees of response. One of these 10 patients was treated because of pressure pain in the rectum which developed due to a sudden increase in the size of the prostate. The patient who had been under estrogen treatment for more than 1 year was relieved of pain following irradiation of the pituitary and improvement coincided with renewed regression of the primary lesion. Improvement has been sustained so far 9 months after completion of x radiation. The remaining 9 patients were subjected to irradiation over the pituitary because of resurgent pain due to bony metastases. All of them had been castrated previously. Temporary relief from pain lasting from 1 to 3 months was accomplished in 6 of these cases and in 3 other cases improvement has been sustained up to the time of writing (4 7 and 9 months). In 1 patient who responded with temporary improvement of pain renewed transient relief was obtained by a second course of x radiation.

It has been our experience in all cases that irradiation of the pituitary produced neither an appreciable decrease in the serum acid phosphatase activity nor increase in the patient's weight or improvement in the appearance of metastatic bone lesions. It is our impression however that some degree of palliation was accomplished and that the rapid downhill course in delayed failure patients was slowed down at least temporarily in some of the cases treated.

Irradiation therapy of the pituitary does not substitute for castration or estrogen administration. These experiments represent

TABLE I—COMPARED VALUES

	Normal pregnancy Javert Stander	Normal control King	Abortions Javert Stander	Abor- tions King
Vitamin C level, average—mgm			25	
Vitamin C—percentage deficient	50		69	
Prothrombin time, average—%	92	81.5	84	61
Prothrombin time—percentage deficient (90% or less)	5	14	7	5
Prothrombin time and vitamin C—percentage deficient			6	5

Since pathological changes do play a large part in abortion both partners, whenever parenthood is undertaken should be enjoying the best possible health in the hope of avoiding any fetal or maternal defect that might result from organic disease. Thyroid dysfunction should be corrected, secondary anemias treated, deficiency states supplemented by dietary and medicinal courses, and organic lesions eradicated wherever possible.

The study for this present report is based on a series of 100 cases composed of two groups: first 82 patients who had already aborted or were inevitable abortions and second 18 patients with threatened abortions. The control group was made up of 35 unselected individuals in general good health. Fifty-two per cent in this series had prothrombin values of 70 per cent or less (method of Quick) and were classed as deficient as compared with 7 per cent found deficient in Javert and Stander's series (method of Warner, Brinkhous and Smith). The average prothrombin time for the cases of abortions in this series was 63 per cent as compared with Javert and Stander's determination of 54 per cent. Twenty-one per cent of this abortion series had deficient vitamin C levels of 0.5 milligram or less (method of Abt and Farmer) as compared with 69 per cent of Javert and Stander's series with deficient vitamin C (method of Mundlin and Butler). Further more this series of abortions was found to have an average vitamin C level of 1.0 milligram as compared with 0.35 milligram in the Javert and Stander series. Fifteen per cent of

the cases of abortions were deficient in both vitamin C and prothrombin time as against Javert and Stander's value of 61 per cent.

These compared values may be studied at a glance in Table I.

It was further seen as appears from Table I that the control determinations on 35 patients with no evidence of nutritional deficiency or hemorrhagic disease revealed 13 per cent had a deficiency in vitamin C and that 24 per cent fell below 70 per cent in their prothrombin time as compared with 21 per cent low vitamin C and 52 per cent low prothrombin time in this abortion group. This type of control was used because Javert and Stander's statistics already reveal a significant difference between the cases of abortions and normal pregnancies.

It may be observed that in general this series of patients showed less abnormality than the series studied by Javert and Stander and that the two studies diverge furthest in the vitamin C levels and the combined deficiency of vitamins C and K.

Lubin and Waltman report that, if one abortion has previously occurred there is only a 70 per cent chance of a later pregnancy going to term in the same mother and that if two abortions have previously occurred, the chance drops to 30 per cent. In this series 11 per cent were primiparas, 47 per cent had no previous abortions, 22 per cent had 1 previous abortion, 9 per cent had 2, 6 per cent had 3 and 5 per cent had 4.

As various authors have stated syphilis does not play a prominent role in abortions in accord with this only 2 patients in our series were positive for syphilis on serologic examination.

Although the incidence of induced abortions in this series was recorded as only 3 per cent, it is believed to have been higher with the true history concealed. Hamilton for example, reports an incidence of mechanical interference in 10.3 per cent of 502 cases and states that a history of previous spontaneous abortion supports evidence that the present one is spontaneous unless admitted induced.

Thyroid dysfunction as determined by metabolic rates in the first 3 months of gestation does not appear to be a great cause of

trouble. Only 6 low basal metabolic rates of minus 15 to minus 30 were noted and 6 of plus 14 to plus 26 in the whole series of 100 cases. When there does happen to be evidence of a low basal metabolic rate in the patient thyroid medication may be of value either as prophylaxis or as therapy during threatened abortion if it comes before the end of the fourth or fifth month after thus the physiological increase in metabolic rate should already be established.

Javert and Stander's therapy consisted of a full nutritional program, supplementary foods to supply vitamin C and K, administration of vitamin C and K if the blood levels were low, mineral supplement of iron and manganese, vitamin B (240 milligrams monthly) when the vitamin C and prothrombin values were low and progesterone and thyroid when indicated. Their results were similar to other reported successes such as those treated with progesterone by Mason, oral pregnenolone by Krohn and Harris, oral anhydro-hydroxy progesterone by Soule and vitamin E by Lubin and Waltman—all about 80 per cent successful.

The results obtained in treating 18 threatened abortions in this series were not so encouraging as the 80 per cent results of other reports. Forty four per cent of this group of 18 aborted and 56 per cent subsided. Seventeen per cent of this group were deficient in vitamin C and 27 per cent deficient in prothrombin time, values which were not noticeably abnormal since this group closely resembled the values of the control group. Only 1 of the 8 cases of the threatened group which aborted had a low prothrombin time and none had deficient vitamin C. In those threatened abortions which subsided 40 per cent had low prothrombin time and 30 per cent had low vitamin C values. Of the 8 threatened abortions which terminated 6 had received vitamin E, 6 of the 10 which subsided had not received vitamin E. Of the 10 threatened patients treated with supplementary vitamin E, 6 aborted. These statistics though taken from a fairly narrow base suggest that vitamin E in large amounts does not prevent abortions.

Therapy consisted of sedation, progesterone and vitamins C and K when indicated. With

the use of proklot, a synthetic water soluble vitamin K, the prothrombin time may increase as much as 5 per cent daily under a dosage of 2 milligrams given three times daily. If the drug is given after meals it is effective without additional bile salts if there is a normal biliary function. Ten of the group were given 50 milligram doses of vitamin E two to four times daily supplied as eprolin, a distilled natural tocopherol.

Lubin and Waltman have reported 80 per cent cures with vitamin E, using much smaller dosage than was used in this series. It is now generally conceded that morphine is contraindicated in threatened abortions because of its oxytocic effect on the uterus. Small or moderate doses of progesterone are usually preferred because of the possibility of destroying the intrinsic supply if large dosage is given.

If the threatened group, 3 or 17 per cent were primiparas which was comparable to the 11 per cent incidence of primiparas in the entire series. Two of these 3 patients aborted and had no deficiency of vitamin C or of prothrombin time. Strangely enough there was a higher incidence of abortions in those without previous abortion history in the threatened group than there was in those having already had one or more abortions though of course this is too small a section of the series to be statistically reliable.

CONCLUSIONS

1. Disease of the fetal or maternal parts is probably present in a high percentage of abortions as indicated by the studies of Hertig and Sheldon (4) and of Paine.

2. In cases of inevitable and of complete abortions, prothrombin time and vitamin C determinations have been lower than in controlled determinations of normal pregnancies and unselected individuals in good health.

3. In cases of threatened abortions, there was found no appreciable difference in the vitamin C level and prothrombin time between the threatened group and the control.

4. Pregnancies showing abnormal bleeding tendencies either by previous history of abortion or by active bleeding during gestation should have vitamin K and vitamin C studies and deficiencies corrected.

were treated with drugs. They have also produced convulsions by placing sulfathiazole on the cerebral cortex (36 37) Other workers have confirmed the above findings in rabbits (21) and in humans (48) although one author (18) reports that convulsions did not occur when sulfathiazole was applied to the brain of cats

The reports describing the effect of the sulfonamides on the peritoneum are conflicting. Some authors (19 29) state that sulfanilamide does not cause any gross or microscopic change in the peritoneum of dogs. Other authors (31) state that there is no reaction with sulfanilamide or sulfathiazole but that there is marked reaction with sodium sulfathiazole. On the other hand sulfathiazole, sulfanilamide and sulfadiazine used in various forms produce adhesions in dogs, sulfadiazine producing a much greater local reaction than sulfanilamide or sulfathiazole (4 9). A fibroblastic foreign body reaction when sulfanilamide suspended in saline was injected intraperitoneally into mice has been reported (11). By employing various sulfonamides and studying the cellular changes in the peritoneal fluid in rats, it has been found that there is a meager response to sulfanilamide and a violent response to sulfapyridine. The author here thought that these were non-specific and depended on a foreign body reaction of the tissues toward the drug itself as well as the innate irritant properties of certain of these compounds (45). One group (46) reported a favorable deposit of fibrin in gastrointestinal anastomoses in dogs when crystalline sulfanilamide is placed along the suture line.

In human beings sulfanilamide and sulfathiazole have been used locally in clean operative wounds (7 8 26 28) in compound fractures (6 23 24 27 33) in traumatic wounds, and war wounds (5 22 34 38 39). The reporters observe reactions varying from no retardation of healing to delayed healing in 50 to 75 per cent of the cases (1). Delayed healing which occurs when the drugs are used in large amounts and leads to the collection of serosanguineous fluid (8) and to clot formation (30) could be avoided by not placing the drug between the skin edges and by reducing the amount of drug used (2). One author in a

clinical observation of over 60 cases states that in 'muscle and fascial layers the sulfonamides appear to delay healing by their chemical effects on cell proliferation and by their presence as foreign material' (15). Peripheral nerve damage has occurred in humans following the injection of sulfanilamide or the use of large quantities of sulfanilamide in wounds (5).

Only a few microscopic studies have been performed on human subjects. Veal and Klepser took biopsies from over 70 chronic ulcers. They noted that prolonged use of sulfanilamide may retard healing by inhibiting cellular growth and by retarding the vascularization of the granulation tissue. On the other hand Rea who studied tissue excised from the edge of infected wounds, usually decubital ulcers, found no gross or microscopic evidence that sulfanilamide interfered with the normal physiology of healing. Well and associates studied sections of tissue from wounds that had been treated with sulfathiazole. Specimens from indolent wounds, from compound fractures at the time of removal of bone plates and from cases of healing osteomyelitis, were examined. Except for the occurrence of foreign body giant cells surrounding crystals of sulfathiazole in a case of osteomyelitis these authors found no evidence that the local use of sulfathiazole contributes to delay of wound healing.

Since the reports in the literature regarding the effect of sulfonamides on tissues and on wound healing are conflicting and since the conclusions drawn from animal experiments are not always applicable to human beings, we decided to study the effects of sulfanilamide and sulfathiazole on human tissues by microscopic examination of the wounds.

MATERIALS AND METHODS

Volunteers were obtained among the hospital patients. The skin of the back was cleansed and under local or general anesthesia two identical incisions were made in the paravertebral region. The incisions were approximately 2 centimeters in length and extended down to the paravertebral muscles. From 0.15 to 0.2 of a gram of sulfanilamide or sulfathiazole powder that had been sterilized by



Fig. 1. Focal area of necrosis about sulfathiazole at 3 days (arrow). Hematoxylin and eosin.



Fig. 2. Wound at 5 days. Note incomplete healing. Hematoxylin and eosin. $\times 65$.

heating in an oven at 140 degrees Fahrenheit for 30 minutes was placed in one of the wound beds. The other wound was used as a control. Both wounds were closed with fine silk. At intervals varying from 1 to 28 days both wounds were completely excised. The specimens were immediately placed in 10 per cent formalin for

fixation and then imbedded in paraffin. Sections for microscopic examinations were cut and stained with hematoxylin and eosin.

RESULTS

Generally the sulfonamide treated wounds had a broader scar than the controls. The



Fig. 3. Excised wound containing sulfanilamide at 5 days. Epidermal bridge has formed. Wound edges are partially necrotized. Hematoxylin and eosin. $\times 65$.

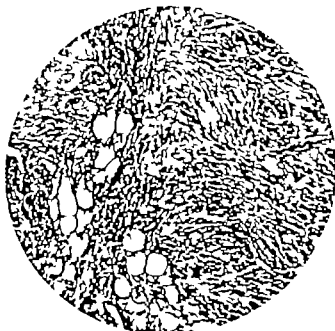


Fig. 4. Control wound at 11 days. Note that almost complete healing has taken place. Hematoxylin and eosin. $\times 65$.



Fig. Wound th sulf thiazole t 1 day. Degree of healing comparable to that of control specimen. Hematoxylin and eosin.



Fig. Control specimen t 1 day. Note that complete healing has taken place. Hematoxylin and eosin.

depth portion of some of the sulfathiazole wounds that were excised during the first week was found to be separated by gelatin until it was not seen in the control wound.

Microscopic examination of biopsy specimens taken within a week after the experi-

mental wounds were prepared revealed a marked leucocyte exudate and focal areas of necrosis in the deep layer of the dermis and in the subcutis of the wounds in which sulfanilamide or sulfathiazole had been placed. Often granules of the implanted drugs provoked a foreign body reaction though frequently the reaction was of a more acute nature. Fibroblastic proliferation appeared to be slightly delayed in the wounds that had been treated with sulfathiazole or sulfanilamide. Since epithelial proliferation occurred promptly in both treated and control wounds casual gross inspection led to the assumption that the wounds were healing with equal rapidity.

Examination of wounds excised 7 to 15 days following their preparation showed healing to be comparable in all wounds. In a few instances some evidence of infection and foreign body reaction was evident in the wounds in which the drugs had been placed. The fibrocyte proliferation appeared equal in all the wounds, and collagen production was uniform.

All of the wounds excised approximately 3 weeks after preparation exhibited almost complete repair.

From a study of the excised biopsy specimens it is evident that sulfanilamide and sulfa-

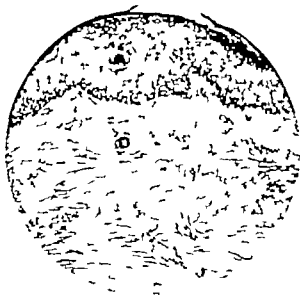


Fig. Wound th sulfathiazole t 23 days. Complete healing th focal area of inflammation. Hematoxylin and eosin, $\times 125$.

thiazole act as irritants to the dermis and the subcutis. In addition they may produce local areas of necrosis and marked leukocytic response in the adjacent tissues. However the deleterious effects are short lived and are not evident in wounds 7 to 10 days old. Subsequent healing is prompt and within normal limits.

It is apparent that surgeons who employ the sulfonamides in wounds must be willing to accept an increased inflammatory reaction about the wound and an initial delay in healing. These undesirable effects can probably be minimized by the use of small amounts of drug in the microcrystalline form. In quantities of the sulfonamides especially sulfathiazole are placed in wounds large irrigations tend to form that are absorbed slowly. Under these circumstances the inflammatory changes here described might be accentuated.

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CONGENITAL ANOMALIES IN THE REGION OF THE UMBILICUS

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THE region of the umbilicus is the site of a wide variety of congenital lesions. Although the incidence of these disorders is not high their pathogenesis is of unusual interest. As the true understanding of any congenital lesion is dependent on a knowledge of the embryology of the region concerned the embryologic aspects of the subject will be considered first.

EMBRYOLOGIC CONSIDERATION

If one examines a 1.5 millimeter (3 week old) embryo it will be found that the greater part of the specimen consists of extraembryonic membrane namely the chorion amnion and yolk sac. These structures although important in the protection and nourishment of the developing embryo are shed at birth. The early relation of these structures to the embryonic plate (future embryo) is shown in Figure 1 A. The early embryo is represented by an ectodermal disc (the embryonic plate) the margins of which are continuous with the amnion. This latter structure is folded over the embryonic plate as a sort of hood and is also ectodermal. Ventral to the embryonic plate and in close contact with it is a saclike structure the primitive entodermal vesicle or yolk sac. The amnion and the yolk sac (which are separated by the embryonic plate) lie together in the large cavity of the primitive blastocyst. The wall of this blastocyst that is the trophoblast later contributes to the formation of the chorion. Only a part of the circumference of the chorion is shown in Figure 1.

Suspending the amnion yolk sac and embryonic plate from the inner surface of the trophoblast is a pedicle like mesenchymal structure the body stalk. Blood vessels are soon formed in this body stalk. These convey

fetal blood to and from the placenta which develops later from the chorion. The mesenchyma of the body stalk is continued over the surfaces of the yolk sac and amnion completely enveloping them (Fig. 1 A). In addition it is insinuated between the ectoderm of the embryonic plate and the entoderm of the yolk sac. Thus three principal germ layers, ectoderm entoderm and mesoderm (derived from the mesenchyma) are intimately associated at the site of the embryonic plate. At the other end of the body stalk the mesenchyma is continued over the inner surface of the blastocyst and constitutes the inner layer of the chorion. The space bounded by this mesenchyma, that is the cavity of the chorionic vesicle is the primitive or extraembryonic celom. The cells which line this cavity form a definite epithelial layer called 'mesothelium'.

Figure 1 B shows an embryo at a slightly later stage. The amnion has increased in size at the cephalic end. It has enveloped the head of the embryonic plate in a hood and then has progressed in a caudal direction and formed the head fold. To a less extent the same process occurs at the caudal end forming the tail fold. By the time the embryo is 6 millimeters long (5 weeks old) the amnion has almost completely enveloped what is now a rather well defined embryo (Fig. 1 C). Only a small circular area where the yolk sac and body stalk enter the ventral surface of what now may be termed the true embryo is not so enveloped. At the margin of this circular area (the future umbilicus) the embryonic ectoderm is continuous with the amniotic ectoderm.

As the amnion is undergoing these changes, the entodermal yolk sac also is developing along certain lines. In Figure 1 A the yolk sac is represented by a nearly circular cyst the top or vault of which is in close relationship to the ventral surface of embryonic plate from which it is separated only by the embry-

Abridgment of thesis submitted by Dr. Trimincami to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of requirements for degree of M. S. Surgery. From the Division of Surgery and the Section on Surgical Pathology M. J. Chase.

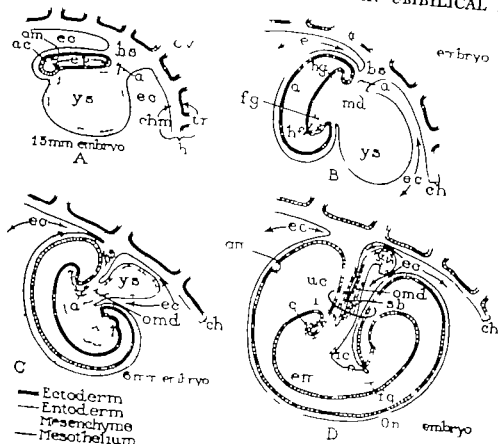


Fig. 1 The development of the structures in the region of the umbilicus. a, allan; ac, amniotic cavity; am, amnion; bs, body stalk; c, clonca; ch, chorion; cm, chorionic mesenchyma; ec, extra-embryonic celom; em, embryonic plate; fg, foregut; hf, head fold; hg, hindgut; ic, intra-embryonic celom; omd, omphalomesenteric duct; sh, small bowel ("herniated" into embryo); tr, trophoblast; uc, umbilical cord; ur, umbilical vesicle; ys, yolk sac. (Modified from Jordan and Kindred, 4th ed. New York: D. Appleton-Century Co., 1942, p. 10, Fig. 104.)

onic mesenchyma. This subembryonic vault of the yolk sac is the primordium of the future digestive system and cloaca. The foregut and hindgut are soon formed from this vault. With the enveloping growth of the amnion the wide communication between the yolk sac and the developing gut is gradually encroached on so that by the time the embryo is 6 millimeters long (Fig. 1 C) this communication is represented by a narrow tubular structure. This is the omphalomesenteric or vitelline duct.

As the amniotic sac grows the omphalomesenteric duct and the body stalk, which enter the ventral surface of the embryo, are pressed close together and elongated. The amnion finally becomes closely applied to these structures and with them forms a tubular organ which suspends the embryo from the inner surface of the chorion (Fig. 1 D). This tubular structure is the umbilical cord.

The yolk sac and the omphalomesenteric duct should be considered to lie from the earliest stage within the extra-embryonic celom. This is the cavity of the chorionic vesicle. In the development of the umbilical cord, as outlined previously, a portion of this extra-embryonic celom is folded in with the yolk sac and the omphalomesenteric duct which come to lie in an extension of the extra-embryonic celom into the umbilical cord (Fig. 1 D).

The intra-embryonic celom or celom proper is the true body cavity. It is formed early by a splitting of the mesenchyma within the embryo. It also is lined with mesothelium. Within it lies the growing gastrointestinal tract. This body cavity is in communication through the umbilicus with the umbilical portion of the extra-embryonic celom. The omphalomesenteric duct is still in wide com-

and is usually found in adults. No opening can be detected and there is no covering of mucous membrane. It can be successfully treated by cauterization or by local excision and cleanliness. An umbilical granulation is seen occasionally after the cord comes away. It consists of a small soft red tumor composed of true granulation tissue. The tumor arises from that portion of the umbilical cord proximal to the ligature which in the process of separation has not come away completely. Local application of the cautery will remove the lesion. Urachal anomalies also must be distinguished from a completely patent omphalomesenteric duct. The fistulous tract of a patent urachus is directed toward the bladder and urine may escape from it. The oral administration of methylthionine chloride (methylene blue) may help to establish the diagnosis of a patent omphalomesenteric duct. Barium injected through the umbilical opening may demonstrate the fistula after a regular barium meal has failed to do so.

The treatment of a completely patent omphalomesenteric duct is surgical. The only operation that yields permanent relief is complete excision of the fistulous tract from the umbilicus down to within about 1 centimeter of its junction with the bowel. The stump is then turned in and closed. The mortality associated with such a procedure should be low.

Partially patent omphalomesenteric duct. As shown in Table I different portions of the omphalomesenteric duct may remain patent in different cases. Failure of the peripheral portion of the omphalomesenteric duct to close produces an umbilical sinus. Findings in such cases resemble those in cases in which a completely patent duct is present. Intestinal drainage never occurs at the site but there is always a mucous secretion or weeping from the sinus. The canal from the red external nodule passes into the abdominal cavity for a variable distance before it ends blindly. The enteric end of the canal sometimes terminates in a fibrous band which is attached to the surface of the small bowel. Occasionally a history of intestinal obstruction is obtained in cases of umbilical sinus so that the possibility of such a band should be kept in mind.

Undoubtedly patency of the peripheral portion of the omphalomesenteric duct frequently has been diagnosed as a simple umbilical concretion or granulation and treated by cauterization. If the sinus is only a few millimeters deep local cauterization might cure it. In most cases, however surgical excision is indicated.

A vitelline cyst is due to failure of the intermediate portion of the omphalomesenteric duct to become obliterated. The cyst may be situated in the wall of the ileum; it may be situated in the abdominal cavity and attached to the ileum or to the umbilicus or to both of these structures, or it may be situated in the anterior abdominal wall. The incidence of proved vitelline cysts is not high. The wall of the cyst usually is lined with an intestinal type of mucosa and sometimes is made up of an intestinal type of submucosa and muscularis. The contents are as a rule a clear mucoid fluid derived from the mucosa. As this secretion accumulates the cyst increases in size the mucosa becomes stretched and flattened and may eventually be unrecognizable as such. The symptoms of these cysts depend largely on their size and location. Small cysts may be present and cause no symptoms especially when they lie deep in the abdomen. Those lying in the abdominal wall may be detected by the presence of a visible and palpable cystic mass. When treatment is indicated the only satisfactory procedure is complete excision.

Patency of the enteric portion of the omphalomesenteric duct that is, Meckel's diverticulum is a comparatively common anomaly. It is found in about 2 per cent of all cases studied at necropsy. Although this anomaly is related to the early development of the umbilicus, it is not strictly an umbilical anomaly. The subject has been dealt with exhaustively by many authors and will not be gone into here.

Remnant of mucosa of omphalomesenteric duct at the umbilicus (umbilical 'polyp' or nodule). A small portion of the omphalomesenteric duct may persist as a bright red mucosal tag or nodule in the umbilical depression after the cord has come away. It might easily be mistaken for an umbilical concretion or gran-

ulation. However it secretes mucus and on microscopic examination intestinal mucosa is found. Unlike the umbilical sinus it possesses no central canal and thus provides the chief distinguishing feature between the two conditions which of course are closely related embryologically. The differentiation of the two may be of some importance from the standpoint of therapy as the mucosal remnant may always be successfully treated by simple cautery whereas the sinus may demand more extensive surgery.

Congenital band (obliterated omphalomesenteric duct) A congenital band arising from the antimesenteric surface of a loop of small bowel to the inner surface of the umbilicus may represent an obliterated omphalomesenteric duct, a persistent (usually the meso-) omphalomesenteric artery, or a fistula. Here again there is always the danger that the intestines may become looped or kinked about the persisting band and may cause intestinal obstruction. For this reason the anomaly when it is found should always be excised. In accomplishing this it is always wise to treat the enteric stump of the band as a patent tube and ligate it firmly as it may contain a minute canal which communicates with the lumen of the bowel.

Urachal anomalies Urachal anomalies arise in the course of development of the bladder. In the following paragraphs the subject will be dealt with from the point of view of earlier writers who believed that the urachus is formed by a process of obliteration of that portion of allantois which extends from the apex of the primitive bladder to the umbilicus. This will be followed by a brief review of Begg's explanation.

Completely patent urachus A completely patent urachus appearing as a fistulous communication between the bladder and the umbilicus at birth is rare. The anomaly is noted as soon as the cord comes away. Often there is a small granular tumor at the base of the umbilicus. The urachal opening may be the size of a pin point or much larger. If the canal is probed the instrument is carried down in the direction of the bladder. The flow of urine from the umbilicus may be in large or small amounts depending on the

caliber of the fistulous canal and on the ease with which urine can escape through the urethra. The flow of urine may be intermittent because of intermittent blockage of the urachal canal. Such blockage usually is caused by infection. Mild irritation of the skin around the umbilicus is common but is of different degree from the severe digestion of skin that is associated with a completely patent omphalomesenteric duct. No pain or discomfort is associated with a completely patent urachus if infection is not superimposed. Frequently the opening of the urachus into the bladder may be seen with the cystoscope.

The acquired type of umbilical urinary fistula is more commonly than one that is present at birth. In the acquired type no abnormality of the umbilicus is noticed immediately at birth but some time later on an irritation begins to dribble from the umbilicus. These acquired fistulas are almost always associated with an obstructing lesion of the urethra such as urethral stricture, hypertrophied prostate gland or tumor of the neck of the bladder. The resulting urinary obstruction forces urine through an incompletely obliterated urachal channel and thus gives rise to an acquired umbilical urinary fistula.

The only satisfactory treatment for a patent urachus is surgical excision of the fistulous tract and closure of its opening into the bladder as permanent spontaneous closure of a fistula of this kind is extremely rare. Before surgical treatment is undertaken the patency of the urethra must be investigated. If obstruction of the urethra is present it must be relieved as a preliminary procedure. The dissection of the fistulous tract should begin at the umbilicus. If opening the abdominal cavity can be avoided the risk of the operation is minimized. Sometimes however the peritoneum is so adherent that the abdominal cavity has to be opened. Injection of methylene blue into the tract may be of assistance. After the urachus has been freed completely it then is severed a short distance above the bladder and the stump is inverted and closed by a pursestring suture.

Partially patent urachus In cases in which the peripheral portion of the urachus has per-

sisted and is patent an umbilical urachal sinus opening at the umbilicus exists. The sinus passes for a variable distance down toward the bladder. The primitive urachal epithelium is believed to possess secretory cells and in these sinuses there is usually a clear mucinous secretion. Persistent umbilical drainage after the cord has come away usually first draws attention to the condition. An umbilical urachal sinus sometimes may begin as a urachal cyst which subsequently breaks through to the exterior at the umbilicus and establishes a sinus.

An umbilical urachal sinus is a local condition which can be successfully treated by local excision. Care should be taken to excise the whole tract. Ordinarily excision of the sinus tract is a simple procedure as the tract lies extraperitoneally. However in many cases infection is, or has been present. Infection increases the difficulty of dissection and frequently necessitates opening the peritoneum. This procedure then increases the risk of operation.

A urachal cyst which is the result of a patency of an intermediate portion of the urachus is one of the commonest congenital anomalies of the urachus. Luschka stated many years ago that the urachal canal usually is completely obliterated and that the normal state is for numerous cystlike cavities (Luschka's lacunae) to persist throughout life. Urachal cysts may be large or small, infected or non-infected. Small cysts may not give rise to any clinical symptoms and usually are found incidentally. However some urachal cysts reach huge proportions. In Rippmann's case the cyst which contained 52 liters of fluid is probably the largest one on record. The increase in size is usually gradual. In some cases there seems to be an intermittent communication with the bladder and in these the size may vary when these cysts empty and fill through this opening.

The wall of these cysts varies from one that is thin to one that is more than a centimeter thick. The inner surface is usually smooth. Most authors have stated that the lining is a transitional type of epithelium similar to that of the bladder but in many cases this lining has become so modified that the original archi-

ture can scarcely be recognized. Only occasional small islets of epithelium may be found. The fluid contained in the cysts may resemble ascitic fluid or it may be tenacious andropy. At other times it has a typical chocolate color which is suggestive of an old hemorrhage.

The first sign of an urachal cyst is usually an enlargement of the lower part of the abdomen in the midline. Sometimes a definite cystic mass may be demonstrable. As the cyst increases in size it may weigh down on the bladder and cause urinary symptoms. It never produces systemic symptoms unless the cyst becomes infected.

Most urachal cysts when they come to the attention of the doctor are in the infected stage. Pain, tenderness, and induration in the lower part of the abdomen are associated with fever, malaise, and sometimes severe prostration. The skin overlying the cyst may be inflamed and indeed the abscess may rupture through it. Usually however the abscess if it ruptures will do so at the umbilicus which may be considered its weak spot.

Urachal cysts must be distinguished from other lesions that may produce a cystic mass low in the abdomen. Cystic remnants of the omphalomesenteric duct may be difficult to distinguish without exploration. A distended bladder should be recognized easily with the help of a catheter. Ascites can be diagnosed by paracentesis. An ovarian cyst lies further back in the abdominal cavity. Localized peritonitis from any cause may be difficult to rule out, but valuable assistance may be obtained from the history.

Since neither simple nor infected urachal cysts disappear spontaneously, surgical treatment is usually indicated. If the cyst is uninfected and small it may be shelled out extraperitoneally. The risk of operation for this type of cyst is minimal. If the cyst is large the peritoneal cavity almost always must be opened in the course of its removal but if the cyst is not infected even then the risk of operation should be small. It is wise to treat the remaining urachal cord extending from the cyst to the bladder as a pervious cord and ligate it firmly, thus forestalling the possible development of a urinary fistula. If the cyst

is infected the operation is a more serious matter. Complete local excision almost always will necessitate opening the adherent peritoneum widely and this procedure under these circumstances is attended by considerable risk. A safer procedure is to incise the cyst widely, curette the walls if they are thick and then pack the cavity lightly with gauze. The gauze is withdrawn gradually. Although this method entails a more lengthy convalescence during which time the wound must heal by secondary intention the safety of the procedure recommends it.

In some cases a persistent vesical portion of the urachal canal communicates with the bladder. The cystoscope may reveal the opening into the bladder. The persistent portion of urachus often becomes cystic because of intermittent occlusion of the opening into the bladder. Infection of this cystic cavity is likely to occur. When infection does take place vesical and constitutional disturbances will appear.

If the anomaly consists of a simple uninfected persistent vesical segment of the urachus often the condition causes no symptoms and no treatment is required. However if the urachal lumen has become cystic the persistent portion probably should be excised and the opening into the bladder should be closed. If the cyst is thought to be infected it is often advisable to isolate, ligate and divide the occluded portion which communicates with the bladder. This procedure then is followed immediately by incision and drainage of the cystic cavity which may be treated like an abscess that has been drained. Closure by secondary intention will follow.

Begg's explanation. Begg (3) stated that the urachal canal is never completely obliterated and in this respect he is in agreement with Luschka. The lumen he found is usually tiny and may become plugged here and there with desquamated cells. In a third of his specimens he was able to demonstrate a communication between the urachal lumen and the bladder. He was of the opinion that although patent the lumen of the urachus is so small that only the most minute quantities of urine can traverse it. He stated that it is lined with a transitional type of epithelium.

Begg explained the genesis of congenital umbilical urinary fistulas in this way. The upper portion of the ventral cloaca fails to narrow and thus a true functional bladder reaches to the umbilicus that is no urachus is formed. If the allantois is patent or if a portion of the vesical wall is involved in the slough of the umbilical stump urine will escape at the umbilicus when the cord comes away. The condition then is a vesicoumbilical not better than a patent urachus.

As for congenital urinary fistulas Begg stated that there are two types: neither type is due to a patent urachus in the usual sense. In the first type no urachus has been formed and the apex of the bladder remains at the umbilicus. Perinatal obstruction, trauma or infection later in life may cause a fistula to open at the umbilicus. In the second and more common type a more or less normal urachus is present. From one cause or another usually urachal obstruction urine is forced through the narrow urachal canal and bursts from its distal end into the space between the transversalis fascia and the peritoneum. It then may burrow its way toward the umbilicus and rupture through the umbilical depression.

Begg was of the opinion that the so called cysts of the urachus may be formed from epithelial cells set free if and when the urachus is torn asunder by the pull of the bladder during the latter's descent into the pelvis. An other origin of urachal cysts may be segments of the urachal canal itself.

Vascular anomalies. Persistent omphalomesenteric vessels. As a rule the omphalomesenteric vessels disappear before birth except for those enteric portions which go to make up the superior mesenteric artery and portal vein. Occasionally however they persist to an abnormal extent sometimes independently and sometimes associated with a remnant of the omphalomesenteric duct. When they are associated with a remnant of the omphalomesenteric duct the vessels may be patent. When an umbilical nodule or polyp is excised blood sometimes spurts from a small vessel which may well be a persistent omphalomesenteric artery. Sometimes these vessels persist as a solid cord running from the mesentery of the small intestine



Fig. 2. Section made through the umbilicus in case in which the urachus was patent. The transitioned squamous epithelium of the skin is seen at the point where it merges into the intestinal type of glandular epithelium of the persistent urachus (hematoxylin and eosin, $\times 24$).



Fig. 3. The lining of urachal cyst, which is composed for the most part of flattened epithelial cells. In one area there is suggestion of multiple layers of cells somewhat like the transitional type of epithelium (hematoxylin and eosin, $\times 50$).

across the peritoneal cavity to the inner surface of the umbilicus or they may be attached at one end to the small bowel the other end floating free.

Persistent umbilical vessels. The umbilical vessels converging at the umbilicus, persist normally as the two obliterated hypogastric arteries and the ligamentum teres of the liver's falciform ligament. It is doubtful whether this process is ever subject to pathologic aberration.

Persistent urachal vessels. Little of significance regarding this anomalous condition can be found in the literature. The urachal artery is normally obliterated before birth. Begg stated that in cases of congenital urinary umbilical fistula the urachal artery persists and causes increased vascularity of the first part of the umbilical cord. This prevents the onset of the dry gangrene which normally causes separation of the cord and a red granular tumor projecting from the umbilicus results.

Somatic anomalies. Somatic anomalies arise from a failure of varying degree in the development of the anterior abdominal parietes. Included in this group of anomalies is the interesting condition of umbilical endometriosis.

Congenital umbilical hernia. Simple umbilical hernia is a condition frequently seen. In these cases, there is a defect in the fascia

and the muscles around the umbilicus so that a peritoneal sac of variable size covered by fat and skin protrudes through the base of the umbilicus. The defect may be due in some instances to a congenital defect in the abdominal parietes. A more likely cause of the common type of umbilical hernia however is in the severe stresses and strains (crying coughing and so forth) imposed on the umbilicus soon after birth at which after all, there is a fresh wound. The subject has been dealt with in many surgical texts and will not be discussed further here.

Of more interest from the embryologic standpoint, although much rarer is the condition known variously as omphalocele ex omphalos amniotic hernia, and evagination at the umbilicus. These numerous names apply to the same fundamental condition. It occurs because the primitive intestine in the embryo fails to return completely into the abdominal cavity from the celom of the umbilical cord long before birth or this return is effected only partially. This failure of the bowel to return wholly or in part to the abdominal cavity may be related to retardation in the development of the abdominal cavity. Ahlfeld however suggested that omphalocele is caused by an abnormal persistence of the omphalomesenteric duct which anchors the intestines out in the cord. The

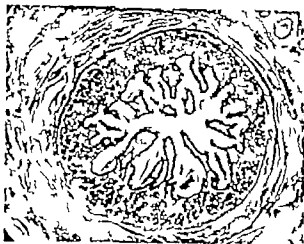


Fig 6 Section through the peripheral portion of persistent omphalomesenteric duct. The typical mucous membrane should be noted. Deep to the mucosa, eosinophilic cells similar to the parietal acid secretory cells of the stomach may be seen (hematoxylin and eosin $\times 3$).



Fig 7 Higher magnification of the eosinophilic cells shown in Figure 6 (hematoxylin and eosin $\times 37$).

at the menses and may rupture through the overlying skin and cause periodic bleeding. Microscopically they show the typical picture of endometriosis elsewhere. Local excision will eradicate the local lesion. If it is part of extensive pelvic endometriosis for which oophorectomy or irradiation is done, the local condition at the umbilicus will of course disappear with the endometriosis elsewhere.

STUDY OF CLINICAL MATERIAL AND COMMENT

A study of the material available at the Mayo Clinic was conducted (9). This study was confined to congenital lesions at or in the immediate vicinity of the umbilicus, such as fistulas, sinuses, cysts and so forth. Umbilical hernia, endometriosis and extrophy of the bladder were not included. Twenty-four suitable cases were found.

The diagnosis in a small proportion of these cases could not be made with absolute certainty because of inflammatory and other changes in the specimen studied. In other cases the nature of the lesions made exact differentiation between two closely allied conditions impossible on pathologic grounds alone. In these cases however clinical surgical and pathologic data together usually permitted the making of a fairly certain diagnosis. The probable anomaly in these cases is given in Table II. A number of interesting

and instructive features were encountered in this study. These will be summarized briefly.

It was found that intra-abdominal anomalies conditions related to the development of the umbilicus may exist with little or nothing to indicate their presence yet these may later be the cause of serious trouble. Each type of anomaly has a fairly characteristic clinical picture but in some cases the characteristic clinical picture was not encountered. In connection with the fact that microscopic examination of the surgical specimen sometimes failed to establish an absolute diagnosis, an interesting observation was made by one of us (J. R. M.). When the urachus persists at the umbilicus the presence of epithelial elements of transitional type would be expected. In several of our cases in which the urachus had persisted at the umbilicus, the epithelial elements were found to be of the glandular type (Fig. 2). If it is recalled that the allantois and urachus originate in the primitive entodermal hindgut, this finding

TABLE II —TYPE OF ANOMALY PRESENT IN TWENTY FOUR CASES

Anomaly present:	
Completely patent omphalomesenteric duct	1
Patent peripheral portion of the omphalomesenteric duct	4
Vitelline cyst	
Mucosal remnant at the umbilicus	
Congenital band (obliterated omphalomesenteric duct or persistent thrombosed omphalomesenteric vessels)	
Completely patent urachus	
Patent peripheral portion of the urachus	4
Urachal cyst in the vicinity of the umbilicus	5

should not occasion undue surprise. The occurrence of primary colloid adenocarcinoma in the bladder illustrates the same relationship to a primitive embryologic type.

Urachal cysts seldom exhibited squamous epithelium of the typical transitional type. On the other hand neither did they have an intestinal type of mucous membrane lining that found in the urachal remnant at the umbilicus. The usual finding if the epithelium had not been destroyed by inflammation was a single layer of flattened epithelial cells (Fig. 3). In one case a cystic mass measuring about 3 centimeters in diameter and lined with intestinal type of mucosa contained pancreatic tissue (Figs. 4 and 5). In another case a section through the peripheral portion of a persistent omphalomesenteric duct revealed a lining of mucus secreting glandular epithelium (Fig. 6). Deep in the lining epithelium lay many glandular acini made up largely of cells resembling the parietal or acid secreting cells of the stomach (Fig. 7). Thus the multipotentiality of the primordium of the omphalomesenteric duct is illustrated.

One case of primary adenocarcinoma of the umbilicus was found in our series. Adeno-

carcinoma of the umbilicus occurs occasionally. It almost always is a metastatic growth which originates in an intra abdominal lesion (stomach, small bowel, liver and so forth). Occasionally however as in one case studied by us an adenocarcinoma of the umbilicus is found which in the light of all available evidence seems to be a primary lesion. The two possible explanations for the occurrence of this type of lesion are: (1) metaplasia from squamous epithelium in the umbilicus and (2) glandular metaplasia in the umbilicus from which the tumor arises. We feel that the latter is the more plausible explanation.

One patient in this series died of peritonitis following the late stage excision of an infected urachal cyst. Care should be taken therefore in the selection of surgical procedures for urachal cysts. Anomalies of the umbilicus usually however find themselves to surgical treatment sufficiently thorough procedure is required. Acute or chronic umbilical hernia which is a common condition in the region of the umbilicus follows.

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SURGERY IN OBSTINATE MEGACOLON

Radical One-Stage Resection and Ileosigmoidostomy

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MANAGEMENT of patients with Hirschsprung's disease or megacolon is frequently difficult. The magnitude of the pathological changes that may develop is classically illustrated in the report by Bach, Imberman, and Kearns. In some patients with obstinate megacolon the bowel perforates during an impaction episode and they die with peritonitis. Abdominal distention in others produces respiratory embarrassment and at times pulmonary and cardiac complications. Also not uncommonly patients enjoy relatively good health with minor inconvenience over long periods of years. Since megacolon is a relatively rare disease the experience of any one individual is based upon observation of a small group of patients and upon information gained from literature studies.

Finney, Eiss, and de Takats and Biggs have summarized the mortality rate associated with medical management of megacolon. These three reviews cover the experiences of 9 authors who individually report mortality rates varying from 19 to 79 per cent averaging 58 per cent. These statistics and the not infrequent autopsy reports of death from complications of megacolon would indicate that, although patients with advanced pathological change can be controlled during long periods of time, they may eventually develop trouble during obstructive episodes. The dangers inherent in protracted conservative management of the more obstinate and progressive forms of megacolon seem to justify colon surgery.

Colon surgery has been described and recommended by Finney, Neugebauer, Eiss, and more recently Yeazell and Bell, Whitehouse, Bergen and Dixon and many others.

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The approaches have varied from simple cecostomy or colostomy to resection of the entire colon and rectum (Bruening). Local resection of the more involved segments of colon has been the procedure usually employed. The mortality rate of this form of surgery before the advent of modern methods of preoperative and postoperative care, modern anesthetics, intubation decompression techniques, and chemotherapy was high. Many of the earlier authors, nevertheless, believed that the risk of surgery was lower in the more severely afflicted patients and the benefit greater than could be expected from medical management. Segmental colon resection is frequently followed by recurrence of extensive involvement of the remainder of the large bowel.

The observation of Royle and Hunter that obstinate constipation in spastic patients was corrected by sympathectomy initiated the widespread use of sympathectomy for true megacolon. Literature studies indicate that sympathectomy may facilitate medical management. It seems well established, however, that the gross pathology of the megacolon is little altered and that many patients again have impactions and occasionally volvulus and that some have died. Yeazell and Bell, Whitehouse, Bergen and Dixon, and others have reviewed and summarized the currently developing opinion that sympathectomy may facilitate medical management of patients with early or mild colon enlargement, but that it is of little avail and perhaps actually harmful in patients with advanced forms of the disease.

A report by Tiffin, Chandler and Faber well illustrates the occasional failure of medical management and sympathectomy. Their patient developed progressive dilatation of the bowel proximal to the sigmoid until at autopsy

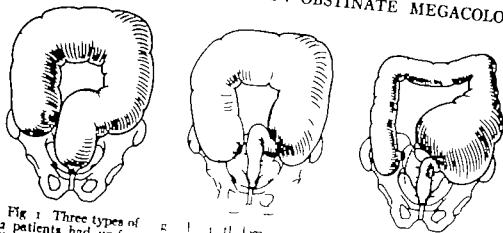


Fig. 1. Three types of megacolon. Group I—dilatable rectum. Group II—terminating in the sigmoid colon. Group III—ascending colon with or without dilated lower sigmoid and dilated rectum.

the ascending transverse and descending colon were uniformly dilated and hypertrophied. Most of the sigmoid colon and rectum were normal. Death of this patient at the age of 20 months and other reported early deaths caution against refusing colon surgery in all obstinate megacolons occurring in infants or young children.

The extent and location of the colon enlargement determines the type of resection that may be employed. Finney and Neugebauer described the incidence of involvement of part or all of the colon and greatly influenced early surgical thought. Finney states that in more than one third of the patients in his review the sigmoid alone was involved. The whole of the large intestine was enlarged in 15 per cent. The rectum was rarely involved. Neugebauer reviewed the early literature and summarized the anatomical findings in 169 patients. The sigmoid alone was involved in 74, the entire colon with all or part of the rectum in 13, and the whole colon without the rectum in 32. The more recent observations of Whitehouse, Bagen and Dixon indicated that in 26 patients the sigmoid and rectum were involved in 4, the sigmoid rectum and descending colon in 4, the sigmoid and descending colon alone in 4, the sigmoid descending and transverse colon in 7, the sigmoid descending transverse and ascending colon in 4, and the entire colon and rectum in 3. The discrepancy between the incidence of involvement presented in the

first two and the third report may be partly explained by the inclusion of findings derived from limited surgical exploration during partial colectomy in the first two reports and the extensive use of x-ray diagnosis in the third.

The megacolon literature has not developed the percentage of patients in whom the dilatation of proximal segments of the colon terminates at some level in the sigmoid and leaves a portion of the sigmoid colon and the rectum grossly normal. That this type of pathology does occur is illustrated by frequent reports in the literature describing a subgroup among the megacolon patients as rectal achalasia. The dilatation of the descending colon and the upper sigmoid in this subgroup usually occurred above a normal rectum and some normal portion of the lower sigmoid colon. The operative findings in the 3 patients to be reported at this time demonstrate that this type of pathology may be associated with immense enlargement of all segments of the proximal colon.

The author has reviewed in a contemporary report (6) the observed anatomical and pathological findings and the clinical course of 24 megacolon patients. Repeated examinations of the entire colon by proctoscope, barium or air contrast enemas and occasionally oral barium have demonstrated that in 12 patients uniform involvement of the entire colon terminating in a dilated or easily dilatable rectum occurred. Eleven of these



Fig. 1. Case. Abdominal ray examination (the age of 9 years). The standard 4 by 7 inch ray plates are required side by side to include the entire abdomen. Patient not distressed. Thus the quality of distention (the reason for it) could increase the number of the abdomen another four inches.

patient are now living. Two of them developed a late volvulus of the sigmoid colon that required surgical reduction. One died 3 years after a sympathectomy. Examination revealed a uniform involvement of the proximal segment of the colon terminating in a normal segment of bowel usually in the sigmoid region and a normal rectum in 7 patients. They presented marked abdominal distention. Episodes of impaction and obstruction occurred at frequent intervals. Four received conventional medical management supplemented in one instance by a sympathectomy and died. The remaining 3 developed severe symptoms and were treated by one

stage resection of the megacolon and ileocecal colostomy and are living. They will be discussed later. Examination revealed enormous enlargement of the sigmoid or the sigmoid and descending colon with or without some involvement of the proximal colon and rectum in 5 patients. These patients are now living. Figure 1 diagrammatically represents the three varieties of colon pathology encountered in these 24 patients.

The mortality incidence of 5 patients in 24 is lower than the mortality rates usually reported. This may be explained by the extension of the follow up record of the 19 patients now living only to their present average age of 15 and the treatment by megacolon resection of 3 of the patients now living at a time when serious complications of conventional management seemed inevitable. The effect of sympathectomy in 4 of the 4 patients also confirms the observations in the recent literature. In 2 patients of the Group I variety sympathectomy was performed. One is now living. The other died 3 years after sympathectomy with an acute colon impaction and perforation. Two were of the Group II variety. One died 2 months after operation. One underwent a megacolon resection 1 year after sympathectomy because of a serious impaction episode. The gross pathology was not appreciably influenced by sympathectomy. Medical management was temporarily facilitated in 2 and apparently permanently facilitated in one.

The pathological lesion encountered in this group of 24 patients and illustrated in Figure 1 differs from that previously reported in the literature. The occurrence of uniform dilatation of the entire colon including the sigmoid and the rectum in 12 patients is substantiated by repeated rectal proctoscopic and barium x-ray studies. The occurrence of uniform enlargement of the entire colon and a segment of normal lower sigmoid and a normal rectum in 7 patients is substantiated by detailed examination and confirmed by autopsy in 1 patient and by exploration during megacolon resection in 3. The occurrence of enormous dilatation of the upper sigmoid and descending colon with or without moderate dilatation of the proximal colon and the lower sigmoid

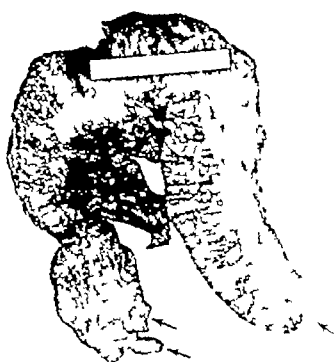


Fig. 3. Case 1. Residual size of thickened terminal ileum and appendix after evacuation and postoperative contraction has to a length of six inches, a circumference of 1 1/2 inches, and an average thickness of the colon wall of five eighths of an inch. The terminal ileum and appendix are indicated by two arrows. The transition between enlarged sigmoid and rectum is indicated by one arrow.

and rectum is clearly substantiated in patients by x-ray evidence.

The difficulties encountered in conventional management of patients of the Group II variety and the serious prognosis have stimulated an evaluation of the effect of a one stage procedure resecting entirely the diseased colon and anastomosing the terminal ileum to the remaining normal segment of sigmoid.

The authors have projected this evaluation of the utility and feasibility of one stage subtotal colectomy with some apprehension because of the experiences of Ladd and Cross. These authors employed this procedure and abandoned it after losing 2 patients from disruption of the intestinal suture lines and peritonitis and a third of the series of 31 years after operation from a perforation of an ulcer of the sigmoid stump. Total colectomies for other diseases have proved successful without anastomosis leaks and without commonly developing late ulceration in the sigmoid. It seems probable that improvements in surgical



Fig. 4. Case 1. Anterior and profile views of patient 1 after subtotal megacolon and ileosigmoidostomy. Three or four mild movements occur daily through the ileosigmoidostomy and rectum. The patient now weighs 150 pounds more than he did before operation.

technique and supportive therapy may reduce the operative risk.

REPORT OF THREE PATIENTS TREATED BY ONE STAGE SUBTOTAL MEGACOLON RESECTION AND ILEOSIGMOIDOSTOMY

CASE 1. This patient was 21 years of age at the time of megacolon resection. Constipation developed shortly after birth and required constant medical management. Early in childhood obstipation and abdominal distention made hospitalization necessary. A diagnosis of megacolon was established. Development was normal except for persistent abdominal distention. A variety of oral medication was employed but found less effective than five days. Five days was the longest time permitted between bowel movements. Ordinarily, movements occurred every day. Episodes of uncomfortable distention were relieved by the

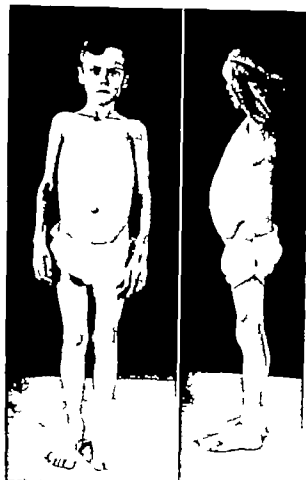


Fig. 5. Case . Anterior and profile views of 10 year old patient with obstinate megacolon 10 days after hospitalization. Large amounts of stool have been evacuated. A sympathectomy was performed.

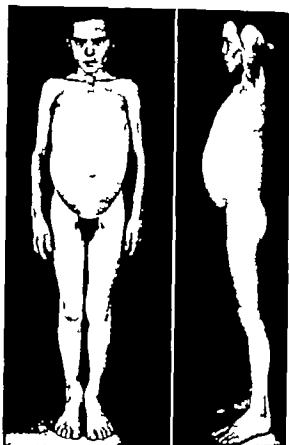


Fig. 6. Case 1. Recurrent abdominal distention 1 year after sympathectomy and 2 hours after emergency treatment directed toward fecal impaction. Large amounts of stool have been evacuated.

patient by lying upon his abdomen and manipulating the palpably enlarged colon through the abdominal wall until expulsion of a large amount of gas had taken place.

At the age of 10 years he entered the clinic stating that the distention he then presented was typical of his usual condition. The magnitude of the residual impaction and distention is represented by the two standard 14 by 17 inch x ray plates necessary for an abdominal study (Fig. 2). The patient weighed 143 pounds and with the exception of his abdomen appeared poorly nourished. During 10 days in the hospital, mineral oil by mouth, d propaner, prostigmine and oil retention and soapuds enemas achieved only moderate relief. He was advised to continue with mineral oil, enemas and a bland low residue diet and was discharged.

Nine months later he was readmitted for 5 days with cramping abdominal pain. The pain subsided after several enemas. He left the hospital with the usual residual distention.

One year later at the age of 11 he again returned stating that mild abdominal cramps had developed and had become more frequent and intense during the day before admission. He insisted that something be done about his colon and requested some form of surgery. Inspection revealed a gigantic abdomen. Strong colon peristaltic waves were visible beneath the vast thin distended abdominal wall. Cautious palpation gave the impression that the contractions of the colon which was visibly 6 or 7 inches in diameter throughout its length would cause a spontaneous rupture.

Rectal examination had at intervals during the preceding two years been interpreted as showing a widely dilated rectum full of feces or a normal rectum. The rectum was now normal in size and empty. Treatment was begun cautiously by employing oil retention enemas. Later as some movements were obtained soapuds enemas, oral cascara and mineral oil, prostigmine and finally after evacuation was almost complete magnesium sulfate



Fig. 7. Case 2. Abdominal x-ray examination after photograph represented in Figure 6. The normal lower sigmoid colon and rectum during the passage of the impaction.

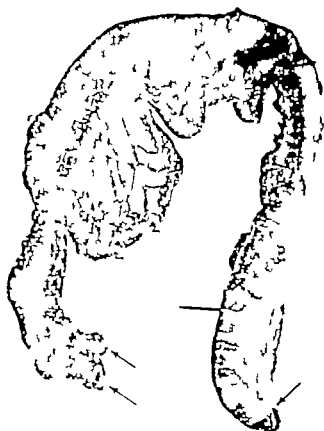


Fig. 8. Diagram illustrating the size of megacolon removed. The megacolon measured 18 inches in length and 6 inches in diameter. The normal sigmoid colon measured 12 inches in length and 2 inches in diameter. The arrows indicate the terminal ileum and appendix. The single arrow indicates the normal sigmoid colon.

and castor oil were employed. The patient was completely emptied of the colon probably within 10 to 15 minutes in many years.

Surgery was then advised and performed under continuous spinal anesthetic. The patient was supported during the 4½ hour procedure by the administration of 1,000 cubic centimeters of 1% lidocaine and 1,000 cubic centimeters of 5% glucose in saline. The abdomen was entered through a 4-inch right rectus incision centered at the level of the umbilicus. The colon was hypertrophied and redundant from the enormous cecum to and including the upper two-thirds of the sigmoid. It measured even in its collapsed state 3½ to 4 inches in diameter. The megacolon was removed by mobilization first of the cecum and then progressively all of the normal colon down to the junction of the middle and lower thirds of the sigmoid. At this level approximately 5 inches above the pelvic floor the dilated hypertrophied colon converted abruptly into a grossly normal sigmoid stump. Care was taken that adequate circulation to this remaining normal colon be saved. The horseshoe shaped area from which the colon had been removed was then carefully peritonealized. The diseased colon (Fig. 3) was removed by dividing the terminal ileum and the junction between normal and abnormal sigmoid. Continuity was re-established by a side-to-side anastomosis between terminal ileum and normal sigmoid

In the inguinal cavity and the abdominal wound was closed. Fine catgut technique was employed. The collapsed and redundant abdominal wall was supported by 6 abdominal pads placed over the wound and held by adhesive taping. The rectum was then gradually dilated manually. The region of transition of large to normal sigmoid colon was carefully examined during exploration and later during pathological dissection. The lumen of the colon was not obstructed.

The postoperative course was uneventful. The highest temperature was 101 degrees. Daily rectal dilations and mineral oil instillations were performed during the first week to prevent back pressure on the suture line. The first bowel movement occurred on the fourth day after operation. Subsequent movements ranged from 1 to 6 a day. Prophylactic chemotherapy employing sulfathiazole, was administered during the first 8 days. Clinical distention, ileus or vomiting did not occur. Moderate distention of areas of the small bowel by gas was demonstrated by x-ray several times during this hospitalization and also 12 months later. These loops have not increased in size.

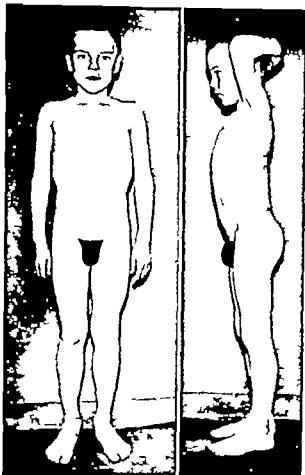


Fig. 9. Case 3. Anterior and profile view of the patient 6 months after resection of the entire megacolon and anastomosis of the terminal ileum to the remaining segment of normal sigmoid. He has gained 8 pounds above his original weight. Soft bowel movements occur 3 to 6 times a day.

The patient returned to engineering school 4 weeks after operation and has carried on normal activities for 9 months. He has gained 45 pounds over the initial weight preceding the evacuation and resection of the colon. Figure 4 illustrates his present condition. Soft semiformed bowel movements occur two to five times each day.

CASE 2. This boy was 11 years old at the time of megacolon resection. Vomiting began a few days after birth. A tentative diagnosis of cardiospasm was made. Some relief was obtained with atropine. At 3½ months of age severe vomiting occurred and a bilateral titis media developed. A few weeks later 6 days passed without a bowel movement and abdominal distention was noted. A diagnosis of megacolon was established. The child was given mild laxatives and frequent enemas. General nutrition remained poor. Pneumonia occurred at the age of 2 and again at the age of 3. At 3½ years diphtheria developed and 14 chicken pox. Despite of

strenuous efforts toward relief of constipation marked abdominal distention and vomiting recurred every 2 or 3 months. The parents gave careful attention to the bowel habit and occasionally used as much as 10 gallons of water during a high colonic irrigation.

The patient was first seen in this clinic at the age of 7 because of constipation, cramping abdominal pain and vomiting. Examination revealed marked abdominal distention and a general state of poor nourishment. The thin distended abdominal wall was distorted by many large fecal masses and by active colon peristaltic waves. Rectal examination revealed an essentially normal rectum without palpable stool. Evacuation was accomplished by medical means during 7 days in the hospital. Depropenex mineral oil and daily enemata were employed.

The patient returned twice during the next year somewhat improved but still poorly nourished. Frequent cuts were observed about the body sustained in numerous fights with the neighborhood children prompted by ridicule of the size of his abdomen. At the age of 10 he returned because of progressively more severe symptoms. One month before this admission the parents were unable to obtain a bowel movement for 30 days. Cramping abdominal pain, severe distention, vomiting, diarrhea, and incontinence had been present during 10 days before admission without relieving the distention. Examination revealed accentuation of the findings observed during the earlier admission (Fig. 5). A large fecal impaction was present just above the rectal sphincter. X-ray examination demonstrated an increase in the enlargement of the colon. The impaction was partly dug out and partly cleared out by mineral oil and enemas and then completely evacuated by oral castor oil.

Seven days after admission the first, second, third, and fourth lumbar sympathetic ganglia were removed and the greater and lesser splanchnic nerves were divided on both sides. The periaortic complex of sympathetic nerves and ganglia was also removed down to and around the origin of the inferior mesenteric artery. The patient withstood the operative procedure well. He was advised to continue with mineral oil and enemas. During the next year daily bowel movements occurred. This satisfied the family. The abdominal distention remained somewhat reduced. The general state of nourishment of the child however did not improve and the defensive fights against ridicule continued.

At the age of 11 a more severe episode of abdominal distention occurred. Three weeks passed without a bowel movement. Because of the interruption of visceral pain pathways effected by the sympathectomy treatment was not requested until enormous distention became obvious and vomiting developed. Within 24 hours the vomiting became fecal. The father brought the child to the hospital believing that he was dying. Examination revealed accentuation of all findings. The vomiting was definitely fecal. The rectum was dilated by hard

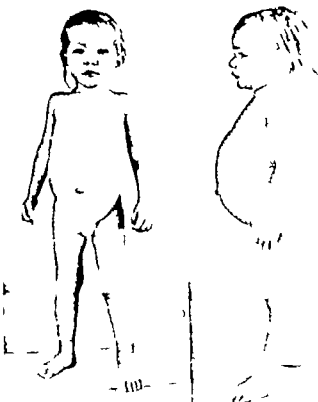


Fig. 10. Case 3. Anterior and profile views of a 20-month-old patient with obstinate megacolon and persistent abdominal distention. Vigorous efforts toward decompression before operation were unsuccessful.

mass of stool which presented at the perineum with the hardness and shape of a fetal head. Intravenous supportive therapy was begun. The impaction was broken up manually. Twelve hours later the boy



Fig. 12. Case 3. Megacolon removed from the patient illustrated in Figures 10 and 11. Preoperative decompression efforts had failed. The arrow indicates the short segment of normal sigmoid colon removed together with the megacolon.



Fig. 11. Contrast radiograph of patient illustrated in Figure 10. The transverse colon down to the sigmoid region distended with gas and fecal material.

was able to pose for a photograph (Fig. 6) and an x-ray plate (Fig. 1). During the next week the colon was gradually emptied by enemas mineral

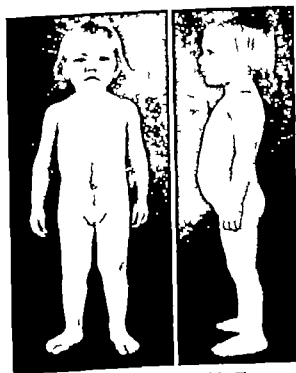


Fig. 13. Case 3. Patient presented in Figures 10, 11 and 12, 3 months after megacolon resection and ileosigmoidostomy.

oil and manual manipulation and finally cleaned out by castor oil and magnesium sulfate.

Colectomy was advised and performed under ether anesthesia. The boy was supported during the 4 hour operation by intravenous glucose and saline and a 500 cubic centimeter blood transfusion. The blood pressure at the completion of the procedure had dropped to shock level but was quickly restored to normal values by additional blood. The operation was essentially that performed in Case 1 except that the midline incision employed for the previous sympathectomy was used and somewhat extended equally above and below the umbilicus. The entire colon was rolled down to a level in the inguinal about 6.5 inches above the peritoneal reflection of the pelvic floor. At this level the enormous dilatation abruptly narrowed down to a normal sigmoid stump. The megacolon was mobilized and after careful peritonealization was resected (Fig. 8). A lateral anastomosis between the ileum and the normal segment of sigmoid was performed. Five grams of sulfanilamide was placed in the abdominal cavity. The rectum was dilated. Pathological examination revealed hypertrophy and thickening of the entire colon down to the mid-sigmoid bowel. The transition from enlarged to normal sigmoid colon was regular without structure or obstruction.

The postoperative course was essentially uneventful. Parenteral prophylactic chemotherapy was employed for 3 days. The highest temperature was 100.2 degrees. Bowel movement began on the second postoperative day and varied between 2 and 6 during the remaining 15 days in the hospital. A large compression abdominal dressing was employed. Abdominal distention did not develop. This boy remained well and active during the 8 months that have elapsed since operation. A letter received 5 months after discharge from the hospital states: "I am well and strong now like the rest of the family. I did not fight at school or at a place at all. The general improvement 8 months after operation is illustrated in Figure 9. He has gained 18 pounds above the preoperative weight. Bowel movements except for one episode of diarrhea vary between 3 and 5 a day. They are soft and partially formed."

This patient occasionally and with difficulty dilated the normal segment of sigmoid colon and the normal rectum during the passage of a fecal impaction. The normal segment of sigmoid colon and normal rectum could have been overlooked by examinations limited to these occasions.

CASE 3. This girl was 26 months of age at the time of megacolon resection. Constipation began at birth and progressively became more resistant to management. Abdominal distention was noted by the third day of life. X-ray examination at this

time revealed distention, chiefly by gas, of the entire colon. Medical treatment was begun. Normal bowel movements never occurred. The baby was hospitalized at 6 weeks of age because of distention, anorexia, vomiting, and diarrhea. A fecal impaction was removed. Colonic irrigation and deprenex gave some relief. Milk of magnesia, prune juice and enemas were employed. At 18 months she was again hospitalized because of distention, vomiting and obstipation. X-ray examination revealed a large fecal impaction of the entire colon measuring 3.5 inches in diameter. One month later the patient was again hospitalized because of persistent distention and increasing resistance to medical management. Some relief was obtained during hospital care and the child was discharged receiving magnesium sulfate dietary management, and colon irrigations. During the next 6 months the abdominal distention persisted. A week at a time would frequently elapse between bowel movements in spite of daily attention by the parents.

The patient was admitted to this clinic at the age of 6 months. Rectal examination revealed a normal rectum and lower sigmoid. The abdomen was distended (Fig. 10) and numerous peristaltic patterns presented through the thin abdominal wall. X-ray examination (Fig. 11) demonstrated a colon distended through its entire length down to the megacolon level by stool and gas. During 3 weeks high enemas, abdominal manipulation, mineral oil, cascara, prostigmine and finally castor oil yielded no return and did not reduce significantly the abdominal distention. During the last week of conservative treatment a duodenal tube was employed. The failure of medical means to reduce the abdominal distention and clear the colon or to maintain adequate nourishment and hydration forced a decision that surgery was indicated. The entire colon down to the transition to normal colon at the junction of the upper and middle portions of the sigmoid was resected (Fig. 12). Either anesthesia was employed. Intravenous saline and dextrose and 400 cubic centimeters of blood supported the patient during the 3 hour procedure. An ileocolic anastomosis was performed and an oblique end-to-end anastomosis was made between the ileum and the normal segment of sigmoid. The technique was otherwise similar to that used in the first patient. Four grams of sulfanilamide was placed in the abdominal cavity. Pathological examination revealed involvement of the entire excised colon. There was no organic obstruction at the point of transition from large to normal sigmoid.

The postoperative course was at first difficult because of difficulty during the first weeks and required intubation. The first passage of stool and gas occurred on the sixth day after operation. Oral feedings when given were poorly tolerated. Distention frequently recurred in spite of the use of intestinal resection and later prostigmine. A barium enema demonstrated that the anastomosis was patent. It was determined that relaxation of the abdominal wall

caused the ileus. A bulky abdominal dressing was pressed tightly against the abdomen by an elastic bandage. The small bowel then decompressed readily. Feedings were well tolerated and bowel movements varied from 2 to 6 a day. The patient was discharged 23 days after operation. She has rapidly regained her strength and weight. Figure 13 shows her condition 3 months after operation. During the 7 months that have elapsed since operation, good health has continued. Four or five soft bowel movements occur daily.

The literature review has demonstrated that protracted medical treatment of megacolon or Hirschsprung's disease may be associated with a high mortality. Surgical intervention is indicated when medical management fails and recurring episodes of serious impaction and obstruction or persistent and progressive abdominal distention develop. Sympathectomy, although it may occasionally facilitate medical management does not appreciably alter the gross pathology. Report of volvulus or impaction and perforation after sympathectomy are accumulating and are attributed in the literature to an overactivity of the large inert colon. The authors believe that the interruption by sympathectomy of the visceral pain pathways that warn patients of impaction and impending danger and provoke strenuous evacuation efforts is a more reasonable explanation of these accidents. Colostomy or cecostomy may be indicated for temporary relief in the occasional patient. Usually however colon evacuation may be accomplished by persistent medical efforts. Segmental colon resection is not uncommonly followed by a recurrence of symptoms of dilatation and impaction in the remaining colon. More radical colon resection would seem indicated if practical.

Three types of megacolon pathology have been encountered by the authors in a case study presented as a contemporary report (6). The patients of Group I with uniform enlargement of the colon and rectum respond well to medical treatment and only occasionally develop difficulty. Should colon resec-

tion be indicated in patients of this group resection of proximal segments of the colon and ileosigmoidostomy would empty liquid bowel content into the remaining enlarged bowel and diminish the danger of recurrence of impaction. Patients of Group II with uniform enlargement of the proximal colon and sigmoid and a normal segment of lower sigmoid and a normal rectum respond poorly to conventional management. Megacolon resection when indicated in patients of this group may be complete. Bowel continuity may be established by an anastomosis between terminal ileum and the segment of normal sigmoid colon. Patients of Group III with immense involvement of the upper sigmoid and occasionally the descending colon apparently respond favorably to protracted medical management.

CONCLUSION

One stage megacolon resection and anastomosis between terminal ileum and a residual segment of normal sigmoid colon have been accomplished in 3 patients. A general improvement in nutrition activity and appearance has occurred.

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SKIN BACTERIA

Their Location with Reference to Skin Sterilization

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IT is well known that there are relatively few bacteria on the surface of the skin immediately after thorough cleansing by mechanical and chemical means. After a short time, however, especially if the skin becomes moist, the number of bacteria increases rapidly and a means of wound infection is created. These additional bacteria presumably arise from the deeper parts of the skin since wound contamination may occur even when the operations are performed under conditions produced by the generally accepted techniques including bactericidal irradiation. The bacteria of the skin fall into two main groups: the transient which may include any organism that comes in contact with the skin and the resident which usually include *Staphylococcus albus* and *Staphylococcus citreus*. It is thought that other organisms may become temporary resident bacteria after prolonged contact with them. These transient bacteria are usually located on the surface and to a large extent can be removed by mechanical and chemical means. The number and kind that make up the transient flora depend on the cleanliness of the individual and his contacts with a variety of sources of contamination including the surrounding air. The resident flora prob-

ably remains fairly constant since over long periods of time the organisms comprising this group have acquired the ability to live and multiply in surroundings that are unfavorable for the growth of other bacteria. It has been assumed generally that they are located under normal conditions both on the surface of the skin and in the deep structures, including the crypts and crevices, hair follicles, sebaceous glands, sweat glands and superficial layers of the epidermis. The purposes of the investigations reported here were to determine the location of the resident bacteria and to demonstrate why the present mechanical and chemical cleansing methods fail to remove or kill these organisms.

EXPERIMENTS

Experiment I. The location of bacteria on the skin

Bacteria studied in sections of skin cannot be recognized to any degree of accuracy because of the small number of organisms and the presence of numerous artifacts. It seemed desirable, therefore, to increase the number of bacteria by incubation in order to locate them readily in regard to their position and depth. The deeper structures of the skin measuring approximately by centimeters in size are obtained from the female breast, pelvis, abdominal wall, scalp, axilla, and lower extremities, for incubation. In one group of experiments these are obtained during the course of routine operations performed under bactericidal irradiation. In a second group of experiments they are obtained from cadavers during the course of autopsies. The skin is cleaned by mechanical or chemical means. In a third group, smaller, topographic specimens are treated by smoothing their surface with a pure culture of *Staphylococcus aureus*. Some of the specimens are then suspended from the covers of individual sterile Petri dishes with the subcutaneous tissue adherent to the inferior surface of the Petri dish cover in contact with the epidermis as thereby voided (Fig. 1). A small quantity of physiological salt solution is placed in the bottom of each Petri dish to prevent drying of the skin. Other specimens are suspended in beef infusion broth. The material is incubated at 37.5 degrees Centigrade for periods varying from 1 to 24 hours. The tissues are then fixed in Zenker's solution, sectioned, and stained for bacteria by modification of the Brown and Brenn method. After incubation for 6 hours, organisms are present in sufficient numbers to make their identification relatively simple. Shorter periods seemed inadequate and longer periods caused an overgrowth in some cases and also caused the tissues to autolyze. The 6 hour period was, therefore, selected for the majority of the studies.

Study of sections from all 3 groups revealed numerous staphylococci located in some of the pilonidal follicles. Organisms could not be seen in all of these structures, and the exact number of bacteria or the number of contaminated

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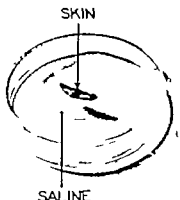


Fig. Photograph showing method used to incubate specimens. The specimen is suspended from the inferior surface of the cover of the Petri dish.

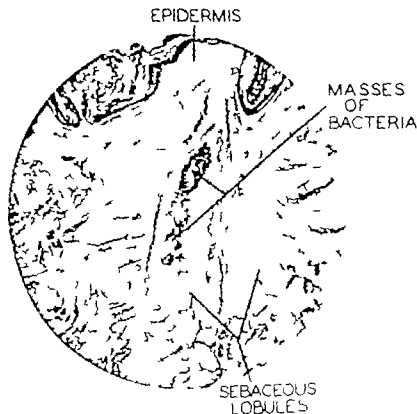


Fig. 2. Photomicrograph showing a section of skin removed from the back of a larva. The surface of the skin was cleaned before removal. The section shows bacteria. Large masses of bacteria deep into the sebaceous glands on the surface.

follicles in any given section could not be accurately estimated because of variations in the direction the section was cut. The number of bacteria and contained in the follicles, however, did not appear to be more numerous in the cleaned skin than in specimens that had been cleaned. Sections of portions of the surface of which had been covered with bacteria before incubation showed no more contamination of the hair follicles and sebaceous glands than those that had been cleaned, comparable sections being examined. This was interpreted as evidence that the organisms seen in the pilonidal follicles of the sections of cleaned skin were resident bacteria. Sections of portions of skin which had been incubated in broth appeared to have more organisms on the surface than those that were incubated in the sterile Petri dish, but they did not have a greater number of contaminated follicles. Perhaps this was due to the fact that the conditions were more favorable for growth.

Sections of cleaned skin removed from a female breast during a routine operation and incubated in a sterile Petri dish served best for study and illustrative purposes; a complete description of these sections follows.

Very few organisms were seen on the skin surface; this was very likely due to the fact that the horny, fatty, rich bacteria are embedded had been removed by the pre-operative preparation and by the fixing and staining reagents. The few organisms that were seen on the surface were between the most superficial cells of the horny layer. Organisms were not seen between or within the living cells of the epidermis. Bacteria were found to be located very deep in some of the sebaceous glands that were cut longitudinally (Fig. 2). The number of organisms in the pilonidal

follicle in the skin of the larva increased sufficiently to fill the pilonidal duct (Fig. 3). Although the organisms around the larval hairs in most sections were present in some of the sebaceous ducts opening in the skin, these structures, in the sections of the skin, in many sections failed to show any bacteria. The excretory ducts in the coiled portion as they pass through the epidermis, in the secreting tubules.

Experiments in the use of surgical cleansing methods for the skin.

Peterson has shown that scrubbing with brush soap, and water removes readily the transient flora of bacteria, but far more slowly the resident flora. As shown in Figure 2, these resident organisms are located very deep in the pilonidal follicles. They are so far below the surface of the skin that they cannot be removed by mechanical means. Sebum is a highly insoluble substance and all of it cannot be removed by soap or chemicals without injuring the skin.

An effort was made to remove the sebaceous material and bacteria from the skin of the hands and forearms by vigorous scrubbing with green soap and water for one hour. After each 5 minutes of scrubbing they were washed in alternate solutions of pure acetone and 70 per cent alcohol for removal and cultures were taken. This procedure failed to remove all the sebaceous material and organisms from the pilonidal follicles. Post-operative cultures were obtained from all 2 specimens, but the greatest number of organisms were removed during the first 10 minutes of the scrubbing time. After the first 10 minutes each successive

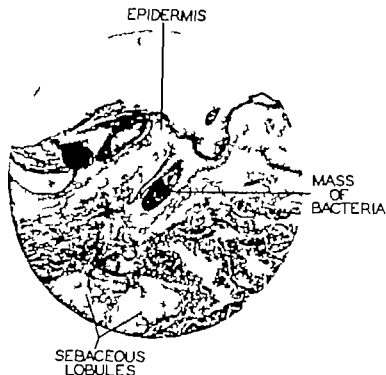


Fig. 3 Photomicrograph showing section of skin removed from the female breast and incubated for 6 hours. The duct of the sebaceous gland is cut in cross section and shows mass of bacteria which fills the lumen of the duct.

cycle of skin treatment caused only slight reduction of surface bacteria as demonstrated by culture.

Any chemical solutions to sterilize the skin must have enormous penetrating as well as bactericidal powers. Some skin antiseptics are used as alcoholic or acetone solutions. The alcohol or acetone, while serving as a solvent for the chemical agent, also is a fat solvent and gives the antiseptic greater penetrating power.

To determine the penetrating power of 70 per cent alcohol and pure acetone the following experiments were performed:

Concentrated solutions of Fehlan (blue fat dye) 70 per cent alcohol and acetone were rubbed gently over the surface of the skin for a period of 3 minutes without allowing it to dry. Frozen sections were then made of the skin, the sebaceous material being left intact. Microscopic examination of these sections showed the depth of penetration of the dye. The greater part of the horny fat on the superficial surface of the skin was stained, but the solutions did not penetrate the pilonidal follicles to any appreciable extent.

OBSERVATIONS

All of the bacteria in our sections were outside of the body since they were not seen within or between living cells of the epidermis or the tissue lining the pilonidal follicles. This is as would be expected if one will recall that the epidermis is considered as an organized structure and all the individual cells

are united with one another either by protoplasmic bridges or by direct approximation. The desquamating superficial cells of the horny layer are not closely adherent to one another and it was between these cells that a small number of organisms were seen in those specimens that were cultured in a Petri dish. The hair follicle is a pouch like depression of the epidermis into the cutis. The duct of the sebaceous gland which is lined with stratified epithelium is continuous with the hair follicle and the inner layers of the hair follicles are continuous with the epidermis. The secretion of the gland is formed slowly and the resident bacteria have acquired the ability to live and multiply in this fatty sebaceous material although conditions are not ideal for growth. The origin of the so called horny fat of the horny cells of the epidermis is unknown but it is possible that the secretion of the sebaceous glands rises to the surface and spreads over the horny layer. It is logical to assume that under normal conditions bacteria are located in this fatty material, the number present depending largely on the cleanliness of the individual. These surface bacteria come from the contaminated sebaceous glands and hair follicles, direct contacts, and air transmitted bacteria.

It appears that bacteria are not located in the sweat glands under normal conditions. During careful study of 175 sections organisms were never found in the sweat glands. It is difficult to obtain sweat without contamination from the surrounding skin. This was attempted however and in several instances sterile cultures were obtained. Sweat is secreted continually from the sudoriferous glands in the form of invisible perspiration (i) The duct of the sweat gland is very small and since sweat is continuously excreted from them it is more difficult for the bacteria to gain entrance to the gland. This is in contrast to the wide open ducts of the pilonidal follicles which are filled with sebaceous material. If bacteria were present in the sweat glands as in the pilonidal follicles they would be more likely to cause infection because of the delicate epithelial lining and the relatively small and tortuous ducts of these structures.

After the skin has been cleaned by the usual methods swab cultures from the surface in many instances are sterile. Later however after the skin becomes moist with perspiration the surface quickly becomes contaminated with a large number of organisms. Despite the negative swab cultures a few organisms are always present on the hands after scrubbing and can be demonstrated by suitable culturable methods. The number of organisms on the skin increase as soon as rubber gloves are placed on the hands and perspiration begins. This increase in the number of organisms is not due to the assumption that they are located in the sweat glands and excreted with the sweat. Rather it is thought that the surface tension is increased when the skin becomes moist and the organisms rise to the surface from their deeper location. In the presence of sweat and a favorable temperature these surface organisms multiply rapidly. Their dormancy previous to attempted skin sterilization also seems to influence the rapidity of growth.

Staphylococci grow best in surroundings having a pH of 7.8. Sweat is mildly acid in reaction. This

acidity of the sweat does have a bacteriostatic influence on the resident bacteria although not sufficient to stop their growth. If cultures are taken after scrubbing and after wearing gloves for one hour it will be found that the number of organisms on the surface has increased during the one hour period. If sodium bicarbonate is added to the hands before the gloves are applied the increase in the number of the organisms will be much greater depending upon the outside temperature the amount of sweat present the frequency of previous scrubbing and the age and dormancy of the organisms present. During the summer months when the surface of the skin remains moist the organisms present appear to respond to favorable surroundings and to multiply faster than older organisms which are dormant on the skin during the winter months.

SUMMARY

Under normal conditions skin bacteria are located on the surface embedded in the horny fat in the crypts and crevices hair follicles and sebaceous glands. Most of the transient organisms of the skin are quite superficial and can be removed by mechanical and chemical cleansing. The resident bacteria are situated so deep in the hair follicles and sebaceous glands that they cannot be removed by mechanical means without injuring the skin. The generally used antiseptics do not penetrate sufficiently to reach the organisms located in the deeper parts of these structures. Although the surface of the skin may be rendered relatively free of bacteria by mechanical and chemical cleansing before operation during operation the resident bacteria rise to the surface multiply and thus constitute an important source of wound contamination.

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TABLE II — PLASMA PROTHROMBIN TIME ON DOGS AND ON RATS BEFORE AND AFTER ADMINISTRATION OF DESICCATED THYROID

Animal	Prothrombin time in seconds of 5 per cent plasma	
	Controls	After 8 days of thyroid administration
Dog	26	24
Dog	17	
Dog 1		20
Dog	29	26
Ra		11
Ra	11	11
Rat 1		

In addition to individual differences in intensity of the reaction there is some difference in the duration of the prothrombinopenic action of dicumarol. However in practically every instance the plasma prothrombin clotting time returned to the preinjection value at about the ninth day after administration of dicumarol no matter whether the dog was receiving thyroid or not.

Table I gives the time in seconds of 12.5 per cent plasma prothrombin clotting time of each of the dogs which were given desiccated thyroid plus dicumarol (group I) and of those that were given dicumarol alone (group II). The average prothrombin times for each of the two groups are plotted graphically (graph I). Both the table and the graph demonstrate that there is no significant influence of desiccated thyroid administration on the prothrombinopenic action of dicumarol in dogs.

After consuming 150 milligrams of desiccated thyroid daily the metabolic rate of the rats on the eighth day averaged 146.5 per cent of the control rate. Dicumarol produced a similar change in the prothrombin level of the rats whose metabolic rate was elevated as it did in the controls. The administration of desiccated thyroid alone had no significant influence on the prothrombin clotting time of either the dogs or the rats (Table II).

The thyroid rats reported in Table II were kept on desiccated thyroid for 15 days and their plasma prothrombin time was taken on the eighth and again on the fifteenth day and no significant change was observed in either case. At about the sixth day there was a noticeable increase in activity and in appetite in the rats receiving thyroid and on the 15th day they had a weight loss of about 50 grams each.

CONCLUSION

The administration of desiccated thyroid has no significant influence on the prothrombinopenic effect of dicumarol in dogs and in rats.

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HEMORRHAGIC SHOCK

The Relative Effect of Amino Acids Amigen and Gelatin in Dogs

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A COMPARISON of the values of saline solution red blood cell saline suspensions, and heparinized plasma in the treatment of hemorrhagic shock in dogs produced by an easily standardized method has been recently reported from this laboratory (11). This paper reports a continuation of the work with comparative tests of pure crystalline amino acids, an enzymatic hydrolysate of casein (amigen) and bone gelatin.

The rôle of parenteral amino acid mixtures and protein hydrolysates in plasma protein production and in maintaining a positive nitrogen balance in human beings and experimental animals has been reported from this and other laboratories (1, 3, 9) and reviewed by Martin and Thompson. This has stimulated speculation concerning the possible rôle of these substances in the treatment of hemorrhagic shock. Elman and Lascher (2) used the survival time of dogs after bleedings of 10 cubic centimeters per kilogram of body weight every hour as an index of the comparative values of a solution of pure amino acids, amigen solution and other substances. The amino acid solution was composed of the 10 essential amino acids in stated quantities totalling 5 per cent in 5 per cent glucose and proved slightly more effective than plain glucose solution. Amigen however proved at least as effective in prolonging survival time as serum or citrated plasma but less effective than heparinized plasma. Toxicity due to citrate was discussed. They conclude that the amino acids and polypeptides of amigen are probably converted rather rapidly to plasma albumin and that amigen is superior to glucose in the treatment of hemorrhagic shock.

Gelatin was first tested clinically by Hogan (1913) but it has not been studied thoroughly until recently. Various objections to its use include the chance of bacterial contamination its alleged antigenicity and hemagglutination effects with possible embolism. Its possible value lies in its large molecular size and its osmotic effects. Robert Robbins, Miller and Whipple (14) have shown that the same gelatin used in our experiments when given by vein to dogs depleted

of hemoglobin and plasma protein gives no immediate toxic effect and no anaphylactoid reactions and may contribute to the building of hemoglobin and plasma protein. When administered intravenously in doses greater than 2 grams per kilogram of body weight it may inhibit the production of new hemoglobin and plasma proteins in these standardized dogs and in larger doses may cause death.

Parkins and associates found that a 6 per cent bone gelatin solution was definitely superior to saline in dogs subjected to single massive hemorrhage or triple hemorrhage. Using prolonged hemorrhage with sustained hypotension these workers found that gelatin and plasma were almost equally efficacious in raising the blood pressure and saving the animals. It was their opinion however that gelatin would fall short of being a complete replacement of plasma if the period of hypotension were prolonged to a point where plasma would not uniformly save the dogs. They noted that gelatin caused more marked hemodilution than plasma and produced a pseudo-agglutination of the red cells. Lawson and Rehm (7, 8) used the change in secondary bleeding volume after a primary bleeding was replaced by the test substance as an index for comparison of blood substitutes. They found that 3-4.5 per cent solutions of a pork skin gelatin and a beef-bone gelatin were much more effective in increasing the secondary bleeding volume than saline and somewhat less effective than heparinized plasma serum and whole blood.

METHODS AND MATERIALS

All dogs used in these experiments were apparently healthy male and female adult animals. They were observed for at least 2 weeks before being used and were fed a diet of hospital scraps reinforced with purina dog chow. Some of the animals which survived were used a second time after a period of 3 to 6 weeks to permit blood constituents to return to normal.

Precisely the same technique was used in these experiments as in the previously reported series saline washed red cells and heparinized plasma being used (11). Briefly the method was as follows: Under local anesthesia the femoral artery

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TABLE III—GELATIN (5 per cent) TRANSFUSIONS

Dog No.	Weight kgm.	Vol. of blood removed	Am. of saline perfused	Vol. re- moved (liters)	Total protein removed		Pre operat. sample		Post oper. saline hematocrit		3 hour sample		6 hour sample		24 hour sample		Observations
					gm	gm / 100 gm	P.P. gm %	Hem- %			P.P. gm %	Hem- %	P.P. gm %	Hem- %	P.P. gm %	Hem- %	
	5	20	20	30		34	5.7				80	3	83	3	5	2.8	Large ma- scale gelatin All survived
38		800	195	4.20	84		6.06	40				5.3	66	0.3	5.3	16.8	
379		700	400	70	3	66	3	26			60	14.7	3.92	6	90	5	
343		300		30	30		97	8	7	3.09		06			60		
304	8	500	26	10	20	60	60		7.6	7.8	5	3.93			37		
		300		700		8	6	45			3.6	8.1			06		
			145	30	58	3.75		30		27			34		60		
307		50			27.5	50		40.6	8.6	30	7		6	69	3.8		
30			26	18.5	7	70	3	46	3	05	5.7		5.5	95	16		
19		700	29	60	5.8	05	5.80						24	6	5.02		
4		60		46			30							5	8	13.8	Small ma- scale gelatin All survived
26			20	100			85		3.8	3.1				8	77		
8			300	30	57.5		66	10.5				05	8	3.01			
		500		100			44			27			19	101			
70				00		64		6			7			5	8		
10		10	24	60		09	1.8		8					49	8		
4		61		4	26	3.77	19.8		8			05	3.4	7	6		

*Posttransfusion plasma solids in analysis

No. 20 Plasma proteins (P.P.)

38 gm. 5%

gelatin

54 gm. 7%

NPN

27 mg. 7%

These dogs had received large scale gelatin at least 4 weeks previously and showed no reaction

heart. There was marked pallor throughout the organs. An occasional microscopic extravasation of blood was seen in the lung. Occasionally liver cells were very noticeably vacuolated.

Masked red cells suspended in a 10 per cent solution of amino acids were given to 6 dogs. The results are shown in Table II. These suspensions averaged 26.6 per cent red cells and had a nitrogen content equivalent to 7.09 grams per cent of protein. Dogs 340 and 358 died immediately and dog 304 died 2½ hours after operation. Dogs 340 and 358 showed fresh blood clots in the pulmonary arteries. Dog 304 had marked hypertrophy of the heart which undoubtedly was of some standing. The 3 surviving dogs showed no reaction. Preoperatively the 6 dogs averaged 5.49 grams per cent of protein and 41.4 per cent hematocrit. Dogs 340 and 304 gave heart blood samples averaging 4.02 grams per cent of protein and 22.5 per cent hematocrit. The heart blood sample hematocrit of dog 358 was 15.2 per cent. There was no apparent hemolysis. The 3 survivors averaged 4.25 grams per cent of protein and 47.4 per cent hematocrits at 3 hours post-operatively. At 24 hours the plasma protein

average had risen to 5.01 grams per cent and the hematocrit average had decreased to 36.7 per cent. The 3 hour hematocrit rise appeared in all 3 dogs. The peculiar drop in hematocrit is noted in the fatal cases of Table II as in Table I. No explanation is offered.

The *red cell suspensions in amigen* averaged a nitrogen equivalent of 6.86 per cent protein and had an average hematocrit of 28.5 per cent. Of 5 dogs tested 4 survived and 1 died as shown in Table II. Dog 380 was found to have dilatation of the heart and heavy round worm infestation involving lungs, liver and kidneys. The 5 dogs had preoperative averages of 5.71 grams per cent plasma proteins and 42.4 per cent hematocrit. Three hours postoperatively the survivors averaged 4.69 grams per cent of plasma proteins and the hematocrit averaged 44.0 per cent. The hematocrit average is affected by a drop in the 3 hour hematocrit in dog 308 whereas, the other 3 dogs showed rather striking increases in hematocrit. At 24 hours the plasma protein figures averaged 4.19 grams per cent. The hematocrits averaged 31.2 per cent. Dog 308 had a marked increase in plasma proteins against a slight de-

TABLE IV—SUMMARY TABLE OF AVERAGE FIGURES

Transfusions	Total blood removed	Bleed- fast per litre- gram	Amount of saline per litre	Blood removed after per- fusion	Total protein removed		Pre- operative samples		3 hour sample (or heart blood)		6 hour sample		24 hour sample		Result
	C.	C.		gm	gm/kg	P.P. gm %	Hem %	P.P. gm %	Hem %	P.P. gm %	Hem %	P.P. gm %	Hem %		
1. no addn 3 dogs	547	4	100	537	4	5.8	5.74	20.8	3	4.8					All dead
2. no addn RBC 5 dogs	505	40	100	50	34.3	3	5.40	4			17	5	6.7	3 are dead	
3. Antigen 4 dogs	720	60	17	320	34.7	4	6		9						All dead
4. Antigen red blood cells 5 dogs	500	4	80	9	5	9	5.7		10						4 alive dead
5. Gelatin 15 dogs	663	4.5	3.7	87	3	1	3.10			0	00		5	All li	
6. Saline 5 dogs	358	53	14	209			6.1	9							3 live dead
7. Washed red blood cells to saline 20 dogs	436	5	20	4	1	3.5	0.6		1.7		3		6	All ali	
8. Heparinized plasma 3 dogs	417	44	3	93	16	1	6.14	10		5		00		1 dead	

(Average 1 less from previous report.)

crease in the others. The only reactions were hives and occasional vomiting immediately after regaining consciousness.

The gelatin results are shown in Table III. All 15 dogs survived. The primary bleeding of all of these dogs averaged about 48 cubic centimeters per kilogram of average body weight.

The 10 dogs receiving the larger molecule gelatin showed a plasma protein average preoperatively of 5.50 grams per cent. Three hours after operation they averaged 4.13 grams per cent and at the end of 24 hours proteins had risen to an average of 4.53 grams per cent. These figures really represent total nitrogen that is plasma protein gelatin, and nonprotein nitrogen. Preoperative hematocrits averaged 43.4 per cent. Three hours after operation the average hematocrit was 14.7 per cent and at 24 hours it had risen slightly to 15.8 per cent.

The 5 dogs which received the smaller molecule gelatin had an average plasma protein level preoperatively of 5.77 grams per cent. Three hours after operation the average had dropped to 3.83 grams per cent and 24 hours after operation to 4.1 grams per cent. The average hematocrit before operation was 39.8 per cent. Three hours postoperatively it had fallen to 15.3 per cent and at 24 hours the average was 13.6 per cent.

Plasma gelatin analyses were made on samples taken immediately after transfusion of dogs 3, 9 and 303 with the small molecule gelatin. The results are shown beneath Table III. The method of analysis was a modification of that described by Janota.

All of the animals in each group recovered consciousness quickly during the transfusion. None showed any sort of reaction even though the last 2 dogs in the small molecule gelatin series had received large molecule gelatin at least 3 weeks previously. All the dogs were able to walk immediately after closure of the wound. All drank well and ate food after operation when offered.

DISCUSSION

A summary of these results and the previously reported results with saline washed red cells in saline and heparinized plasma is seen in Table IV. With saline 3 dogs survived and 12 died in 40 minutes to 18 hours with washed red cells suspended in saline all of 10 dogs survived and with heparinized plasma 11 dogs survived and 4 died in 1 1/2 to 9 hours.

These results indicate that recovery from a massive hemorrhage may be obtained by (1) rapid restoration of the oxygen carrying capacity of the blood or (2) rapid and sustained restoration of the circulating blood volume. Restoration of neither results in high mortality while the fulfillment of either one will yield a low mortality. The ideal is a combination of the two as with blood.

The complete failure of aminocaproic acid to save any of the dogs is unexplained. The unexplained drop in red cell hematocrit in response to it appears that the very rapid injection of these relatively large quantities of hypotonic amino acid solution is not tolerated.

The deaths of dogs receiving red cell suspension in amino acids and amigen may be partially ex-

CONDITIONS SUITABLE FOR TRANSFUSION THERAPY WITH RED CELLS

There may be differences of opinion in some cases as to the choice between red cell or whole blood transfusions. It seems to be the best policy at the present time to leave it to the physician to decide in what instance he wants to give a transfusion of red cells to his patient. The blood and plasma bank of this hospital has supplied red cell suspensions for transfusions on the request of physicians mainly in the following conditions:⁴

1 To supply red cells in anemic patients non responsive to liver and iron treatment.

2 To improve clinical symptoms due to anemia before the effect of liver and iron treatment is established

3 To stimulate and influence organs to function normally. Red cells may have a stimulating effect on megacaryocytes in purpura and on regeneration of red cells in pernicious anemia. Red cells improve the function of organs due to better oxygen supply with improvement of degenerative stages.

4 To bring patients out of danger zone of an extremely low blood count, e.g. acute and chronic hemorrhage

5 To build up anemic patients before and after operation before operation to anticipate hemorrhage which may occur and to turn poor surgical risk into a good one after operation to shorten convalescence

6 To provide replacement therapy in conditions in which (a) cells are continuously destroyed e.g. in lymphoblastomas malignant tumors, hemolytic anemia etc. (b) cells have become insufficient to carry oxygen e.g. in carbon monoxide poisoning lead poisoning erythroblastosis fetalis, etc. (c) the bone marrow has lost power of regeneration e.g. in aplastic anemia, metastases of malignant tumors late stage of lymphoblastomas, etc.

Very frequently red cell suspensions of group IV (O) blood were used for groups other than IV (O) in instances when homologous blood was not available. Group IV (O) Rh negative red cells were used in instances in which Rh negative blood of the homologous group was difficult to obtain. We also have used red cells in some instances in which a transfusion reaction was expected because of the condition of the patient (allergy, hemolytic jaundice, etc.) This was done because of reports in the literature which indicate that reactions are less frequent with cell suspensions than with whole blood (5, 6, 11). MacQuaide and Mollison believe

that reactions might be avoided if the buffy coat (leucocytic cream layer) is removed. The number of such transfusions given in our institution has not been sufficient to be conclusive as to whether or not reactions may be avoided with the administration of red cells.

Most of the conditions mentioned in this survey do not require further comment. However the question comes up whether hemorrhage due to primary or secondary purpura can be safely treated with red cell suspensions. In these conditions, as well as in agranulocytosis, blood is usually given to replace valuable leucocytes and platelets. Although transfusion therapy in general has not been too successful in these conditions cell suspensions may be safely given as long as the buffy coat (leucocytic cream layer) which is extremely rich in leucocytes and platelets, is not removed. This layer will contain an increased amount of these elements when the blood has been centrifuged. However, arrangements should be made that suspensions of this kind are as fresh as possible as quick deterioration of these substances will occur upon storage.

COMMENT ON OBJECTIONS AGAINST TRANSFUSIONS WITH RED CELLS

Red cells often are unnecessary in severe shock, whether from hemorrhage, severe burns, or trauma. Nephritis with edema, nephrosis with albuminuria, dehydration, intestinal obstruction, hypoproteinemias, cerebral edema, postoperative hypoproteinemia, starvation edema, and similar conditions require the administration of plasma.

Not to deprive the patient of valuable proteins seems to be the main objection of physicians against the administration of red cells. The formation of blood proteins is one of the main functions of the liver. There is definite indication that the plasma proteins are synthesized by the liver. This synthesis will be disturbed if the oxygen supply is low. Anemia may be connected with hypoproteinemia and reversal of the albumin globulin ratio due to liver damage because of anoxemia. The rapid increase of the number of oxygen-carrying cells in the body only can benefit the production of plasma proteins, removing the anoxemia and bringing the liver back to normal function if the damage has not advanced too far.

Therefore as long as an anemic patient with a moderate degree of hypoproteinemia is not losing any albumin or the hypoproteinemia does not become any worse, the administration of red cell suspensions cannot be considered contraindicated particularly if supported with a high protein diet.

⁴The results obtained in this hospital correspond closely to those obtained in the previous literature.

or amino acids. In such cases, however it seems preferable to give concentrated red cell suspensions to avoid dilution of the patient's plasma. Cases of anemia with edema are rare and edema may result also from other causes than hypoproteinemia. If the edema is due to heart damage administration of concentrated red cells will limit the fluid given while the greater number of transfused cells may have a beneficial effect due to a better oxygen supply of the organs and especially the damaged heart muscle.

If the edema is due to hypoproteinemia it seems logical to give transfusions with whole blood. There seems to be, however, no objection or damage to the patient when plasma and concentrated red cell suspensions are given alternately and later on continued with red cell suspensions alone, depending upon whether or not the edema disappears. With this more selective administration of red cells and plasma the condition of the patient can be controlled much better and more quickly than with whole blood. The same holds true for patients with chronic blood loss due to bleeding. Blum (3) states there is no danger in giving plasma and administering blood subsequently.

In acute blood loss the reasoning must be different as there is a loss of circulating protein with the rapid loss of blood. If shock is impending preventing it is necessary with the administration of plasma. If the patient goes into shock restoration and maintenance of the total blood volume are more important than getting a normal red cell count. The red cell count can be brought quickly up to normal levels by concentrated red cell transfusions when the danger of shock is removed. The benefit to the patient will be that of accelerated improvement of a condition which cannot be checked with whole blood quickly enough. In case hemorrhage from a peptic ulcer some protein will be reabsorbed in the intestines. However, are too everything must be done to avoid shock in the initial stage of the bleeding.

COMMENT ON SUCCESS OF TRANSFUSION THERAPY WITH RED CELLS

In general it may be stated that success in transfusion therapy with red cells not only depends on the number of cell transfusions given but also on the type given (simple suspension or concentrated cells) and on the time of survival of the cells in the circulation. Concentrated red cell transfusions of course are more effective than simple red cell transfusions. Otherwise, there is

no objection to simple red cell transfusions as saline is quickly absorbed from the circulation. The time of survival in the circulation depends to a great extent on the age of the cells selected for transfusion. Cells must be fresh as storage for more than a few days brings about tendency to deterioration and increase in fragility. (9) Stored cells from which the plasma has been removed hemolyze quickly. Hemolysis can be delayed if a preservative is added. However even then the cells will keep only for a certain period of time. Transfused cells definitely have a tendency to stay longer in the circulation when they are fresh. Until a procedure has been found to make preserved cells as efficient as fresh cells the cell suspensions should be prepared from fresh cells only.

On the other hand the condition of the patient is of the same importance as regards the final success in transfusion therapy with red cells as it is in transfusions with whole blood. Some conditions require repeated transfusion therapy until the patient recovers and until the blood count is elevated sufficiently. In other conditions transfusion therapy must be continued for months or even years. Transfusions with red cells are ideal and economical in such cases.

SUMMARY AND CONCLUSIONS

The plasma reserves of any hospital having the facilities of a blood bank can be increased by the more economic use of whole blood. Suggestions are made as regards conditions which might be treated sufficiently or even better with red cells only and an endeavor is made to disprove some of the objections to the use of red cell suspensions. It is hoped that more frequent use of such therapy is made in the future.

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HEPATICODUODENAL INTUBATION WITH HEPATODUODENOSTOMY FOR TRAUMATIC STRICTURE OF THE HEPATIC DUCT

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THE operation of cholecystectomy is not always a simple and innocuous procedure. It is not devoid of serious post-operative complications, not a few of which may be ascribed directly or indirectly to errors in surgical technique. Serious injury may result immediately or some time subsequently from the accidental ligation clamping or excision of either the common or hepatic ducts during the course of a cholecystectomy. As a matter of fact, in an analysis of 130 postmortem examinations performed in surgical diseases of the biliary tract Colp and Ginzburg reported that about 6 per cent of the deaths could be ascribed either to the immediate effects of operative injury or a subsequent traumatic stricture of the ducts.

The general subject of benign cicatricial stricture of the extrahepatic ducts, their repair and reconstruction has been thoroughly reviewed and discussed by Elliot (4, 5). This communication is concerned mainly with the discussion of the clinical aspects of traumatic stricture of the hepatic duct following cholecystectomy, and a report of 5 such consecutive cases in which the operation of hepaticoduodenal intubation with hepatoduodenostomy was performed.

The history obtained in this type of hepatic duct obstruction does not differ materially from benign strictures of the choledochus. The post-operative course in these cases as a rule is fairly characteristic and follows one of several patterns. After a cholecystectomy bile may drain externally for several weeks or months and then as the biliary drainage gradually diminishes, jaundice, pruritus, acholic stools, and dark urine are noted and episodes of right upper quadrant colic may occur. Occasionally a painless icterus, gradually increasing in intensity, will develop many months after the removal of the gall bladder. Intermittent fever and chills in these cases are not infrequent for the effects of continued biliary obstruction together with infection may result in an ascending cholangitis, cholangitic cirrhosis and finally multiple liver abscesses. As a rule there is

a coincident loss of weight and strength, for marked vitamin deficiencies and nutritional disturbances are the inevitable result of either a persistent external biliary fistula or a complete obstructive jaundice.

The majority of these patients are invariably treated expectantly with the hope that this post-cholecystectomy complication, i.e. biliary fistula or obstruction, may be due to a residual duct calculus which will be spontaneously eliminated. However these patients are eventually referred for surgical exploration when a complete biliary obstruction persists or a fistula drains uninteruptedly for months.

Physical examination as a rule reveals anemia, severe dehydration, evidence of recent weight loss, and, in the presence of biliary obstruction, jaundice of varying intensity. The skin may show ecchymoses and signs of extensive excoriations. The scar of a previous upper right rectus incision, either firmly healed or draining bile, may be evident. The liver is usually enlarged and palpable, and often tender on pressure. The laboratory findings in the blood, urine, and feces are characteristic either of an obstructive jaundice or a complete external biliary fistula.

The adequate preoperative preparation of these patients is most essential if a smooth postoperative course is to be anticipated. Severe dehydration and electrolytic imbalances may be corrected by adequate amounts of fluid orally and parenterally. The lowered protein content of the blood which is invariably present may be elevated by a high protein diet together with adequate carbohydrates. If these oral feedings are not tolerated the addition of parenteral plasma supplemented by the intravenous administration of a 5 per cent solution of amigen may increase the serum albumin and globulin.

The danger of postoperative hemorrhage which formerly exacted a heavy death toll in the jaundiced patient has been practically eliminated by the proper administration of vitamin K, bile salts, and transfusions of blood. The efficacy of these therapeutic agents may be accurately judged by the elevation of the lowered prothrombin time to

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one within normal limits. If this does not occur severe liver damage may be predicated and a many postoperative course often terminating fatally may be predicted.

Secondary operations upon the extrahepatic bile ducts in general and plastic procedures in particular are often complicated and involved problems. They may be very time consuming and productive of shock. Surgical exploration is best performed under continuous spinal anesthesia which produces excellent muscular relaxation and provides adequate exposure. During operation a continuous infusion of 5 per cent glucose in normal saline is administered to which blood and plasma may be added if the occasion demands. The operative findings in these cases are fairly uniform. The intra abdominal adhesions are so firm and dense that at times the lines of demarcation between adjacent viscera appear almost indistinguishable and only sharp knife dissection will delineate their boundaries. The liver and omentum are invariably bound to the anterior abdominal wall and the colon is firmly plastered to the left of the gall bladder bed. The foramen of Winslow is frequently obliterated so that familiar anatomical landmarks are extremely difficult to identify. After the colon is separated from the liver the duodenum is usually found pulled upward. It must be carefully freed from a mass of scar tissue in the region of the porta hepatis. This area, bearing in mind the close proximity of the hepatic artery and portal vein is then carefully explored and aspirated with a fine hypodermic needle (2) for the presence of bile in the syringe indicates the location of the hepatic duct. An incision is then made along the needle as a guide and the surrounding scar tissue is excised thus exposing a shortened and dilated hepatic duct. In case 2, the operation had to be discontinued at this point because the general condition of the patient became so precarious that further surgery was deemed inadvisable. The right and left hepatic ducts were simply drained by separate tubes and the restoration of biliary intestinal continuity was completed at a later date. In cases of long standing biliary obstruction with severe hepatic damage, a two stage operation may be the procedure of choice.

Attempts in these cases to isolate the distal portion of the common bile duct in the gastroduodenal omentum are futile. The defect existing between the choledochus and the hepaticus and the disparity in their lumens would make any type of hepatoccholedochal reconstructive procedure impractical. The ideal operation in this type of case would be a suture hepatocoduodenos-

tomy preferably without intubation. The direct approximation of the mucous membrane of the hepatic duct to the mucous membrane of the duodenum produces the minimal formation of scar tissue. This is insurance against the recurrence of stricture a frequent aftermath in reconstruction of the extrahepatic bile ducts.

Unfortunately in this particular group of cases the existing mechanical conditions at the porta hepatis made it impossible to anastomose the mucous membrane of the hepatic duct to that of the stomach duodenum or jejunum. Therefore biliary intestinal continuity was established by hepatocoduodenal intubation supplemented by hepatoduodenostomy.

Biliary duodenal intubation under these conditions is invaluable. It is a relatively simple and safe procedure. A fenestrated tube of the highest grade of rubber radio-opaque if possible and of sufficient tensile strength and caliber so that it will fit snugly into one of the hepatic ducts, is threaded on a heavy probe and introduced upward into the liver. This single tube with its side holes evidently drains both ducts without difficulty. Its distal end about 8 inches in length is then passed into an opening made into the opposing duodenal wall and directed preferably toward the jejunum. However the tube may be passed through the pylorus and brought out of the anterior wall of the stomach similar to a gastrostomy. Interrupted mattress sutures of linen then approximate the serosa of the duodenum to Glisson's capsule of the liver in the region of the hepatocoduodenostomy. The posterior and lateral sutures are first inserted and tied before the anterior group is placed. This area is then drained by rubber dams which emerge through a separate right subcostal stab wound.

In these 5 cases a complementary jejunostomy for alimentation was performed about 18 inches from the duodenojejunal angle, the enterostomy tube making its exit through a left lateral stab incision. The advantages of a jejunostomy in this type of case need very little comment. Fluids and nourishment in the form of Scott Ivy formula may be administered almost immediately without disturbing the area of the anastomosis. If a biliary or duodenal fistula should develop suction drainage may be instituted immediately. The surrounding skin is thereby protected from the ravages of pancreatic digestion and the chemical balances may be maintained by the introduction of the aspirated duodenal contents through the jejunostomy.

The abdominal wall is then closed in layers with chromic catgut or with heavy through-and-

through silk sutures and the skin edges are approximated with clips.

At the conclusion of the operation, a Levine tube is introduced nasally. This not only maintains decompression of the stomach but the presence of bile in the aspirated contents is an indication of the efficacy of the intubation. Oral fluids are withheld until about the 6th day, nutrition and hydration being maintained parenterally and by jejunal alimentation. As a rule the jejunostomy tube is removed about the 10th day.

The postoperative complications in cases of hepaticoduodenal intubation are either immediate or late. Leakage at the site of the anastomosis may result in a biliary or a duodenal fistula, or a general peritonitis. Drainage has largely eliminated the occurrence of the latter. In Cases 4 and 5 there was a temporary seepage of bile but this soon subsided within a few days. In Case 3 a frank duodenal leak developed which terminated in a right subphrenic abscess and massive empyema with multiple loculations. During the period in which a duodenal fistula was active the secretions were aspirated by the continuous suction of the Steadman pump and chemical balances were regulated by the introduction of the aspirated contents through the jejunostomy. The late complications may be ascribed directly to the intubation or to a recurrent stricture at the hepatoduodenostomy.

The use of the rubber tube undoubtedly has some immediate advantages and a few possible late disadvantages. It assures the prompt delivery of bile into the intestine, automatically relieving the obstructive jaundice. Its mechanical presence not only prevents an edema occluding the anastomotic site but in addition it acts as a supporting scaffold until the union between the hepatic duct and duodenum is firm. In the majority of reported cases, and in ours, the incessant peristaltic activity in the intestine was sufficient ultimately to dislodge the tube which was eventually passed by rectum from 3 to 12 weeks after operation. Some of these patients were unaware that the tube had been eliminated although x-ray examination failed to reveal its presence. On the other hand, the tube may be retained indefinitely. It may subsequently become plugged with bile salts, and then due to poor bile drainage an ascending infection may result. Judd reported the retention of a tube for 4 years when a cholangitis developed which necessitated its removal 2 years later. However innumerable opportunities have been afforded to examine tubes which have been retained in the bile ducts for a year or more. Many of these were found to be in a good state of

preservation and relatively free from the encrustation and disintegrating effects of bile salts. Andrus cited a unique case in which the tube had been in place for 8 years and still seemed to be serving its initial purpose. It would be desirable to control the passage of the tube, but older methods in which this was attempted were discarded because they were unsatisfactory. In Case 2 in which the tube was brought through the stomach so that theoretically it could have been withdrawn at will the early development of a gastric fistula necessitated its removal by the 11th day. The early removal of the tube in this case, at a time before a firm anastomosis had been established was probably the reason for the early recurrence of a stricture. However if tubes of sufficient caliber are used so that they will fit snugly into the hepatic duct, a sufficient time will elapse for firm healing to ensue before the tube is eventually dislodged.

Pearse in order to eliminate some of the objectionable features of rubber used vitallium tubes especially designed to meet the particular mechanical conditions encountered in various types of strictures of the extrahepatic bile ducts. He found that this metal did not corrode and that bile salts were not precipitated on its walls. Experimentally he noted that the mucous membrane lining the tube failed to show any reaction although the mucous membrane did not grow into the metal tube. But he added there was a tendency for all tubes used in this work to pass into the intestinal canal. Sufficient time has not elapsed to demonstrate the advantages and superiority of this type of prosthesis.

The serious complication of ascending cholangitis is always a possibility in any reconstructive procedure in which the sphincter mechanism has either been sidetracked or eliminated. It is probably most common in cases of hepaticoduodenostomy of the type herewith discussed. The proximity of the duodenum to the liver permits the reflux of intestinal contents directly into the bile ducts and if a stricture of the neostomy develops, conditions are ideal for the development of an ascending infection. Yet there are many reported cases of hepaticoduodenostomy in which patients remained well for years. Elliot collected 41 of these cases, in which 11 were free from complications from 10 to 20 years. In this small group there were 3 patients who after the immediate postoperative period never experienced any clinical evidence of an ascending infection. Patient in Case 1 has been well for 4 years, in Case 4 for 15 months, and in Case 5 for 4 months. In Cases 2 and 3 attacks of Charcot fever have been

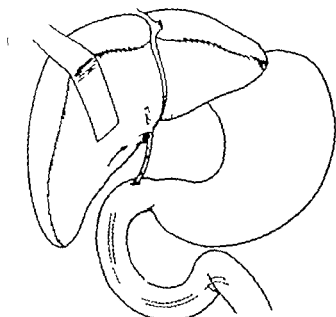


Fig. 1. Case 1. Catheter entering left hepatic duct with side hole to drain the right.

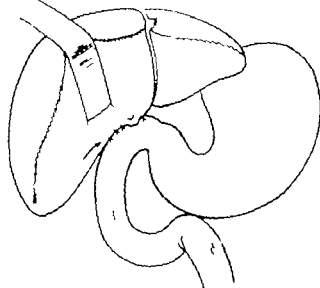


Fig. 2. Case 2. Duodenum sutured to Glisson's capsule by interrupted mattress sutures.

frequent in the former for about 3 years and in the latter for about 18 months. In both a probable recurrent stricture is present. In Case 2 as already stated the tube was of necessity withdrawn too early, and in Case 3 the development of a duodenal fistula probably favored the deposition of excessive scar tissue formation leading to a stenosis of the hepaticoduodenostomy. These symptoms may be partially ameliorated by stimulating intestinal activity and the flow of bile by the judicious use of saline cathartics and the administration of the sulfonamide compounds.

In intractable cases of Charcot's fever it has been suggested that these recrudescences of ascending infection might be eliminated if the gastric contents were completely diverted from the region of the hepaticoduodenostomy. This was done in Case 2. A subtotal gastrectomy of the Billroth II type was performed. No decrease in the incidence of fever, chills, and jaundice was noted and attacks of cholangitis seemed to occur with the same intensity and degree of frequency. Perhaps the infection was so firmly entrenched in the finer biliary radicles of the liver that no palliative procedure at this stage of the disease would have had a mitigating influence on the clinical course of the disease.

CASE REPORTS

Case 1. No 463410, C. M. admitted to hospital October 1, 1940 discharged November 7, 1940. This 35 year old female had had severe attacks of epigastric pain lasting from several hours to days for the past 5 1/2 years. These were usually precipitated by ingestion of fatty foods, but were not associated with vomiting, chills, fever or jaundice. About 1 1/2 months before the present admission

patient was operated upon for appendicitis at another hospital. At the same time the uterus was found to be retroverted and a Gilliam in position was performed. In the course of the abdominal exploration the gall bladder was palpated and found to contain stones. A cholecystectomy was performed through a separate upper right rectus incision. Postoperatively the patient ran a stormy course. There was profuse biliary drainage for 1 week and at this time the stools were not acholic and jaundice was not present. In about 2 weeks the biliary drainage ceased, but this time a mild icterus and itching developed and the stools became clay colored. Since then there has been a progressive jaundice without pain, chills, or fever.

Physical examination revealed an obese, subcutely ill looking woman, complaining of pruritus. The lungs were clear and the heart normal. Pulse rate 96. Blood pressure was 95/58. There was no costovertebral angle tenderness. There were two well healed scars, one suprapubic and the other a right upper rectus. The rectal and pelvic examinations were negative. Hemoglobin was 80 per cent. White count was 6,000 with a normal differential. The Wassermann was negative. The urea nitrogen was 11 milligram per cent the blood chlorides 405 milligrams per cent, icteric index 30, bil rubin 0, and the an den Bergh direct positive. The cholesterol was 355 milligrams, and ester 100 milligrams. The prothrombin index was 00 per cent. The urinalysis showed a plus bile with faint trace of urobilin. The flat plate of the abdomen showed no evidence of stone in the right upper quadrant.

The patient was prepared for operation with intravenous vitamin K (5.2 mgm) and intravenous glucose. Operation was performed on October 10, 1941 under cyclopropan anesthesia. The scar of the right rectus incision was excised. After numerous firm adhesions were freed a mass of dense scar tissue as identified in the region of the porta hepatis. A section of this by means of a hypodermic syringe revealed bile. This mass proved to be a region of the dilated hepatic duct just lateral to a perforated fenestrated rubber tube 3/16 inch in diameter, inserted at the right hepatic duct. The duodenum, which was not adherent to the porta hepatis, was then incised on closely adherent to the porta hepatis. The biliary tube was then removed. The dilated end of the biliary tube as it entered the duodenum was led into the jejunum.

phosphatase level of 38 King Armstrong units. Electrocardiogram showed left axis deviation.

The preoperative clinical impression was that the patient suffered from either residual calculus in the common duct or a stricture in some portion of the extrahepatic biliary system.

Operation was performed under spinal anesthesia and the colon and duodenum were adherent to the under surface of the liver which, after being freed, revealed scar tissue and a definite stricture of the hepatic duct 5 centimeter from the porta hepatis. Liver was enlarged about a finger below the costal margin and appeared cirrhotic. Hepatic duct was slightly dilated. A rubber tube was introduced into the right hepatic duct and its distal portion as led to an opening made in the first part of the duodenum on the superior aspect. The duodenum was found sutured to the under surface of the liver with several mattress sutures. T-tubes were placed in the region of the hepaticoduodenostomy and these were brought out through right subcostal stab wound. Eighteen inches from the duodenojejunal angle a Kader Stamm type of jejunostomy was performed for alimentation. The tube was brought out through left subcostal stab wound as closed with heavy through-and-through silk sutures and pincettes for the skin.

Following operation patient did very well. For the first 48 hours there was profuse drainage along the rubber dams which soon ceased and within 24 hours there was but little Levin tube drainage. The pruritus was definitely less, and the stools showed some bile. The jejunostomy tube was removed on the third day and patient was discharged with wound well healed.

She was last seen July 6, 1944, at which time she had no complaint, no chills, fever or jaundice. She looked well and wound was thoroughly healed.

CASE 5. No. 5775 M. A., admitted to the hospital March 4, 1944, discharged April 24, 1944. The patient, a 5 year old woman, was transferred to The Mount Sinai Hospital from another institution because of persistent obstructive jaundice. Three months previously she had entered that institution with an attack of right flank pain associated with chills and fever and pyuria. Pyelography revealed right ureteral calculus with dilatation of the pelvis and calyces beyond it. A right nephrectomy for a calculus pyonephrosis was performed. Three weeks later the patient returned to that hospital with fever, right upper quadrant pain, nausea, vomiting, jaundice, dark urine and clay colored stools. No previous history of biliary complaints. At exploratory laparotomy the thickened gall bladder contained 3 stones, was found deep to the liver bed. It was removed and a small stone was removed from the choledochum. After irrigation the duct was closed without drainage. Postoperatively the jaundice persisted. One week later second exploration was performed. The common duct was reopened and probed in both directions, no obstructions being met. No explanation for the jaundice was encountered. A catheter was placed in the common hepatic duct, persistent biliary fistula resulting.

Patient was a chronic markedly jaundiced. The public scar and a recent biliary fistula in the lower

Laboratory examination: bile stools were clay colored; white blood count 8,300; total 460, esters 90; cephalin negative; urine bilious; negative; galactose tolerance 3 seconds; blood protein

Patient was prepared for three transfusions of blood for an anteoperative period.

Operation was performed sodium pentothal. When there were found intumescences were small but not cirrhotic as attached. After this found to be due up and the porta hepatis with formation. After the distension the area was aspirated and bile obtained. Stomach tube and dilated hepatic rubber tube was passed side by side draining the left into the duodenum. The stomach to the under surface passed through the Glissoum. Four Penrose drains hepaticoduodenostomy and right subcostal stab wound incision as closed with sutures, prior to which 8 inches from the duodeno-

Postoperative course: appeared the Levin tube operation, and although along the rubber dams, which were given by jejunostomy as the patient was which as about the 6th was removed days after charge the wound was well.

Patient was seen on June absolutely disappeared. It had been no episodes of

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THE USE OF AN IDENTIFYING TUBE IN THE COMMON BILE DUCT IN GASTRIC RESECTION FOR DUODENAL ULCER ADHERENT TO THE BILE DUCTS

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In an operative experience with subtotal gastrectomy for duodenal ulcer now amounting to 500 resections for this lesion, nothing has been more forcibly impressed upon me than that the mortality in this operation, particularly for those who have had considerable experience with this procedure, is perhaps associated more with the relationship of the duodenal ulcer to the common bile duct and its point of entrance into the duodenum than with any one other single factor.

With this fairly good sized experience the technical steps of subtotal gastrectomy have become so standardized that they can be so executed that one does not fear either leakage at the suture line or failure of the anastomosis to function. In very few of our cases are indwelling Levine tubes employed postoperatively and peritonitis has been practically abolished as a complication.

Lethargia, particularly continuous spinal anesthesia, in the hands of those expert in administering and maintaining it, has produced such relaxed and quiet fields that even though the operation may be a prolonged one, shock now rarely occurs. Postoperative suction bronchoscopies enable us to manage the occasional case of postoperative pulmonary atelectasis, has eliminated postoperative pulmonary complications almost entirely.

Fortunately, most duodenal ulcers in patients coming to surgery are located on either the anterior or lateral wall of the duodenum. They so tend to become adherent to the common bile duct or to involve the duct and pancreas in the area of invagination about the ulcer that the common pancreatic ducts in this type of ulcer not only are in danger of being injured as the ulcer is being removed in these partial gastrectomies, but in 3 such cases I have had to transplant the common and pancreatic ducts because of the obstruction present. The indurated area is so low as to require resection of that part of the duodenum into which the ducts enter in order to get enough duodenal stump

for safe closure of the end of the duodenum, a procedure which in my opinion is of such hazard as to be avoided if possible.

When a posterior wall or lateral wall duodenal ulcer erodes, as it often does, into the head of the pancreas or along the outer margin of the duodenum, the scar and exudate so often associated with it markedly shorten the duodenum by scar contracture, and the bile duct is frequently caught in this exudate. This results in considerable distortion of the relationship of these structures to each other and makes it quite impossible for the operator to be sure, as he dissects the indurated ulcer out of the head of the pancreas, that he will not bind, as we all occasionally have found, that with the removal of the scarred duodenum and its contained indurated ulcer, he will be so close to the papilla of Vater that there is not enough duodenum left to turn it in safely. It is possible also that he will find that he has injured the common and pancreatic ducts and is faced with the need of transplanting them.

Although we have always insisted in writing on this subject that the first step of any gastric resection for duodenal ulcer should be a test of demonstrating the relationship of the ulcer to the common duct, it is not always possible in such scar and induration to establish clearly the most important point of this relationship, that is, the course of the common duct as it runs through the scarred and indurated head of the pancreas to enter the back of the duodenum.

I wish again in these occasional problem cases to call attention to the advantages of introducing a "T" tube into the common duct with a long lower limb running well down into the duodenum through the sphincter of Oddi to serve as a means of constantly identifying the location of the duct and its point of entrance into the duodenum. We have illustrated and described the procedure that has proved so useful to us in those occasional cases of low indurated duodenal ulcer, but in given cases such constant demonstration is not out of the pancreas, these cases are very rare, but indurated and adherent to the duct, I have not called attention to it.

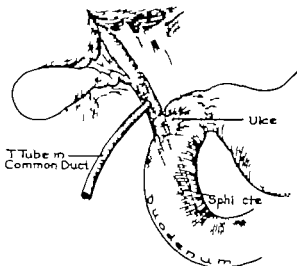


Fig. 1. This illustration attempts diagrammatically to demonstrate the advantages of having a T tube in the common duct when a duodenal ulcer is adherent to the duct and must be dissected from it. By means of this tube passed into the common duct and through the sphincter the relation of the common duct to the ulcer and the location of the sphincter is at all times demonstrable.

With the common duct demonstrated by the duodenum being rotated to the left by traction as we have described, the duct is opened, the sphincter of Oddi dilated with Bakes dilators and a T tube with a long lower limb tightly sutured into the common duct (Fig. 1) so that its lower limb projects through the sphincter into the duodenum.

With such a tube in place one can at all times palpate the tube in the duct and be sure of its relationship to the ulcer-containing portion of the duodenum being removed and at the same time by palpating the point of entrance of the tube into the duodenum, establish the location of the point of entrance of the duct and so by this identification be sure that with the removal of the ulcer-bearing portion of the duodenum, there will still be left enough duodenal stump to close it safely and that as the ulcer is dissected out of the pancreas the duct is not injured.

It is our opinion that with this aid in keeping evident the relationship of the common duct and its point of entrance into the duodenum in the low indurated, and adherent duodenal ulcer it will more frequently be possible to avoid recourse to less satisfactory surgical procedures such as gas-

troenterostomy or Finsterer resections by exclusion. The most satisfactory surgical procedure for intractable duodenal ulcer which we have today is high subtotal gastrectomy with removal of the duodenal ulcer and that portion of the duodenum in which it is located.

In suggesting and illustrating this aid to the removal of duodenal ulcers adherent to the common bile duct, I wish particularly to warn that there exist occasional cases of low duodenal ulcers in which the ulcers are so actively indurated and have so involved all neighboring anatomical structures in the thick white gristle-like scar tissue about them that, even with this suggested aid, it will at times be unwise to remove such ulcers without unjustifiably risking the integrity of the common and pancreatic ducts. It is in such cases that only the operator experienced in these problem cases can determine the possibility of safe removal of such duodenal ulcers with preservation of the ducts. As our own experience has widened we have been able to remove more and more of these adherent ulcers involving the ducts and invading the pancreas, many of which in the past we did not feel capable of removing without undue risk of injury to the ducts. We do not wish to imply that it is necessary to introduce a T tube into the common duct in every patient with duodenal ulcer submitted to partial gastrectomy. This procedure, we believe, should be reserved for those cases in which because of the scarring and exudate, one is uncertain about the relationship of the duct to the duodenal wall and ulcer.

Should there be any serious doubt about whether or not the ulcer-bearing portion of the duodenum can be safely removed as a part of the subtotal gastrectomy for duodenal ulcer we strongly advise the employment of a two stage procedure, anterior gastroenterostomy with the removal of the omentum as we have proposed, or the Finsterer resection by exclusion type of operation, with the understanding that the ulcer bearing portion of the duodenum and the pylorus will be removed at a later date when the ulcer has healed and the induration has disappeared.

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ASEPTIC NECROSIS OF THE CAPITAL FEMORAL EPIPHYSIS FOLLOWING ADOLESCENT EPIPHYSEOLYSIS

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ADOLESCENT slipping of the capital femoral epiphysis is not infrequently followed by occlusion of the blood supply to this epiphysis. This complication occurs as the result of damage to the blood vessels of either the visceral capsule or the ligamentum teres during the period of progressive displacement. It may follow the trauma of surgical or manipulative procedures undertaken to replace and fix the epiphysis in its normal position on the neck of the femur. Subsequent distortion of the shadow of the head, narrowing of the shadow of the articular cartilage and irregular density of the ossification center are usually seen in the roentgenogram. These findings may be accompanied by limb deformity and progressive loss of motion in a varying degree.

The pathology of this complication of the disease has not been reported in detail. It is the purpose of this communication to describe the changes observed in the articular cartilage, ossification center and synovial membrane of two cases of slipped femoral epiphysis followed by aseptic necrosis.

Ky reviewed the descriptions of 24 pathologic specimens of this disease reported in the literature prior to 1926. Of the 24 specimens only 2 instances of necrosis of the epiphysis were reported. In one of these specimens described by Frangenheim, the epiphysis was markedly displaced. The epiphyseal trabeculae were not atrophic as were those of the adjacent living bone of the neck and the lacunae of the epiphyseal trabeculae contained no osteocytes. The second specimen described by Kappis, showed necrosis of the bone and marrow of the epiphysis and replacement of the dead bone by living bone in areas of living fibrous tissue about the periphery. The cells of the epiphyseal and articular cartilage were living. Illustrations of the microscopic pathology are not shown in either of these reports.

Waldenström described the gross changes in the articular cartilage of 3 cases in which he believed necrosis of the epiphysis followed forceful manipulation of the hip under anesthesia. From gross observation he concluded that the articular cartilage

of both the epiphysis and the acetabulum became necrotic. Microscopic evidence was not submitted in support of his claims.

In Suto's report of 3 cases, Case 1 described as a healed slipped capital epiphysis on the left showed no microscopic evidence of necrotic bone or marrow elements within the epiphysis. The illustration of the roentgenogram however shows marked distortion of the shadow of the head with irregular sclerosis and rarefaction of the ossification center which suggest interference with its blood supply. The widening of the shadow of the articular cartilage and lack of ossification of the epiphyseal growth plate suggest the diagnosis of old Legg Perthes disease. The other 2 cases reported by Suto show no roentgenographic or pathologic evidence of interference with the blood supply to the epiphysis.

The synovial membrane in Kappis case was hyperplastic and tended to grow over the margins of the articular cartilage. Howarth described by periphasia and low grade inflammatory changes in the synovial membrane of 70 cases of slipped femoral epiphysis in various stages of displacement which were subjected to arthrotomy.

In adults, Axhausen and Bergmann (2) Phemister (10, 11) and Kahlstrom Burton and Phemister (5, 6) have described in detail the degenerative and reparative changes involving the cartilage and subchondral bone following fractures, dislocations and other idiopathic lesions associated with infarction of bone and cartilage bordering on a joint. Phemister (10, 11) has shown that in adults the necrotic cartilage overlying areas of bone infarction undergoes absorption and replacement by fibrocartilage or occasionally in part by bone. Axhausen (1) has shown that degenerative changes take place in the apposing articular cartilage and subchondral bone several years after necrosis of the cartilage and underlying bone on one side of a joint. These changes in the adult lead to progressive narrowing and reduction of the width of the shadow of the cartilage in the roentgenogram.

During the early growing period the articular cartilage appears to be less dependent upon the circulation of the underlying bone. With interrup-

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tion of the blood supply to the ossification center the synovium may furnish adequate nutrition to the cartilage which continues to proliferate, and thus becomes thicker than normal as in Legg Perthes disease. Restoration of the circulation to the underlying bone leads to creeping replacement of the necrotic bone followed by resumption of endochondral ossification but the shadow of the articular cartilage on the roentgenogram usually remains slightly wider than that of the normal side due to this discrepancy between growth of the cartilage and replacement of its deeper portion by bone.

Even in adolescence near the end of the growth period the articular cartilage may remain alive after devitalization of the underlying bone. However the rate of growth of the cartilage at this age is much slower than that of the younger child and cessation of endochondral ossification may not lead to any appreciable increase in the depth of the articular cartilage as is seen in Legg Perthes disease. In the young adolescent it appears that much of the deeper zone of the cartilage may undergo degeneration and subsequently become ossified after revascularization of the underlying bone. If such degeneration involves much of the deeper portion of the cartilage ossification of this zone may actually lead to narrowing of this structure. These changes are exemplified in the following case in which aseptic necrosis followed slipping of the capital femoral epiphysis in a young adolescent boy.

CASE 1. H. T., 12-year-old boy, jumped from shed 1 year before admission. 1 day his right knee. He continued to play the same day but 4 hours later complained of pain in the right hip, and his parents noted that he limped. Treatment consisted of bed rest for 3 to 4 weeks after which he walked with support. Pain and limp returned, and progressive loss of motion led to hospitalization.

Examination showed marked limitation of motion of the right hip. Flexion as held adduction and slight external rotation. Flexion was possible to 30 degrees, but there was no rotation abduction or adduction.

Roentgenograms of the hips (Fig. 1) show anteroposterior view of the neck of the right femur and obliteration of the inferior half of the shadow of the capital epiphyseal growth disc. The epiphysis of the greater trochanter is closed. These epiphyses on the opposite side remain open. The vertical depth of the right ossification center less than that on the left. There is irregular erosion of the femoral neck and broad zone of juv. isepiphyseal rarefaction. The epiphysis has undergone irregular replacement except for rectangular area in the superior half which has much greater density than has the surrounding bone, indicating that it is vascular and necrotic. Narrowing of the shadow of the articular cartilage and irregularity of the shadow of the cortex or zone of provisional calcification over the revascularized areas are noted. The shadow of the right acetabular cortex is less spherical and regular in contour than the left.

Arthroplasty as performed. When the joint was opened, the parietal and visceral synovial membrane showed

marked villous proliferation. The cartilage surface was fibrillated and faulted but the necrotic portion of the epiphysis was not separated. About 35% of the capital epiphysis was resected in the operation.

A photograph of a portion of the superior half of the epiphysis (Fig. 2) shows irregular ossification of the articular cartilage from beneath over the revascularized area, A. Over this area the cartilage has been reduced to less than 1 millimeter in thickness in places, whereas the cartilage over the uninvaded area, B, measures 3.5 to 4 millimeters in depth.

Microscopically the ossification center (Fig. 2, a) shows vascular fibrous tissue invasion of the marrow spaces, M, which contain areas of necrotic marrow debris, X. The dead trabeculae, R, bone lacunae are empty are being absorbed and replaced by living bone, B. Numerous osteoblasts, osteoclasts, and multinucleated foreign body giant cells are seen throughout the living connective tissue.

The superficial zone of the articular cartilage (H, Fig. 2, b) which is viable and stains normally shows fibrillation and fibrillation. The middle zone, X, stains intensely blue and the cartilage capsules contain living cells. In the basal zone, Y, the matrix is granular and stains poorly except about the capsules. The latter contain necrotic cell debris or are empty. Absorption and ossification of the basal zone above the old zone of provisional calcification, Z, is seen. The depth of the articular cartilage is thus reduced from beneath as seen in the photograph, and cancellous bone replaces the degenerated areas of the cartilage.

The synovial membrane (Fig. 2, c) shows villous formation and marked proliferation of the subintimal connective tissue. The latter is edematous and heavily infiltrated with lymphocytes and plasma cells, many of which are arranged in focal collections. Cultures of the synovial membrane were sterile.

After growth of the epiphysis is complete, the articular cartilage apparently depends more on the circulation of the underlying bone for its nutrition and the changes it undergoes following interruption of the blood supply to the epiphysis appear to be similar to those occurring in the adult with aseptic necrosis of the caput following fracture of the neck of the femur.

These changes in the epiphysis at the termination of the growth period are described in the following case of epiphyseal necrosis occurring after complete traumatic separation of the capital femoral epiphysis. This patient was obviously a case of hypogonadism, and though his chronological age was 21 at the time of admission epiphyseal development of the bones of the hand indicated a bone age of approximately 16 years according to the standards of Todd.

CASE 2. W. M., 21-year-old male, was first seen 6 months after traumatic separation of the right capital femoral epiphysis. Reduction under anesthesia and immobilization for 3 months in plaster casts failed to produce bony union of the epiphysis with the neck. He had not borne weight on the limb since the accident.

Examination showed no evidence of development of the secondary sex characteristics. He was tall, moderately obese, and mentally retarded. A roentgenogram of the hand showed failure of closure of the epiphyseal lines of the mid-

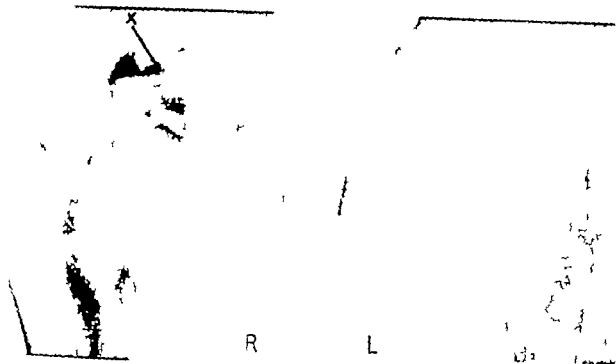


Fig. 1. Case 1. Necrosis following minimal trauma of the right capital epiphysis. The shadow of the epiphysis is narrowed over the revascularized area.

...ent ... by ... of th ... thirds of the epiphysis has been replaced by new bone.

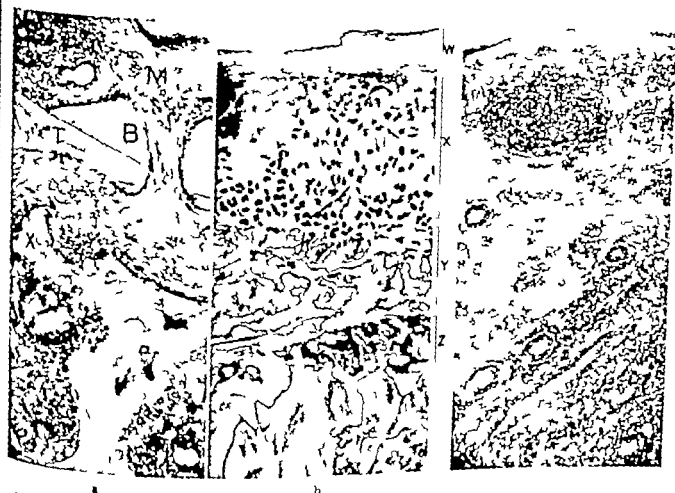


Fig. 2. Case 1. a) Histomicrograph of the revascularized area of the ossification center. X75. b) Section of the

epiphysis ... trabeculae ... large ... Section of the ...



Fig. 3. Case Excised portion of the superior half of the epiphysis. The left half has been revascularized and shows ossification of the basal and midzones of the cartilage

distal and proximal phalanges, metacarpals, and distal end of the radius and ulna.

Röntgenograms of the hips (Fig. 4) show an almost completely separated right capital epiphysis and a healed moderate slip of the left capital epiphysis. The detached epiphysis on the right is more radiopaque than the adjacent living bone of the shaft except for the inferior third and a small wedge-shaped area at the upper pole. The shadow of the articular cortex over these areas is absent, and the shadow of the cancellous bone is more irregular and of finer structure than is that of the adjacent bone. High on macroscopic examination proved to be dead.

The head was excised and arthrodesis of the hip was done. At operation the neck was found to be attached to the epiphysis by adhesions only. The superior aspect of the neck was eburnated where it came in contact with the roof of the acetabulum. The head was adherent and fixed in the acetabulum by adhesions. The ligamentum teres was frayed and torn, and the articular cartilage was badly indented, faulted, and fibrillated. There was overgrowth of pannus from the margins of the epiphysis and forera. The articular

cartilage over the inferior third of the epiphysis was replaced by fibrous tissue and fibrocartilage.

On section (Fig. 5) the central and upper third of the bony center were found to consist of yellowish-white necrotic bone. A small area at the superior pole and the inferior third consist of delicate brownish-red spongy bone.

Microscopic examination of the lower third (A, Fig. 6, a) shows fibrous tissue invasion of the marrow spaces, and phagocytosis of the necrotic marrow elements. The dead trabeculae have undergone partial absorption and replacement by living bone. The overlying cartilage is replaced by fibrous tissue and fibrocartilage, here it came in contact with the lower part of the capsule or foreshadowing acetabuli.

The small area at the superior pole (B, Fig. 6, a and Fig. 6, b) shows absorption of the necrotic articular cortex and creeping replacement of the underlying spongy bone by articular connective tissue. The necrotic articular cartilage is being absorbed by connective tissue from beneath and is undergoing absorption and fibrocartilaginous replacement by pannus growing out from the articular margin above.

The remaining mass of bone and overlying articular cartilage (C, Fig. 6) is necrotic except for small basophilic staining areas of cartilage superiorly (D, Fig. 6) in which the cartilage capsules contain many living cells and the midzone turns tensely thick hematoxylin. The remaining articular cartilage is necrotic except for small superficial areas where surface cells remain alive. Irregular surface absorption of dead cartilage by overgrowing pannus (A, Fig. 6) seen. The underlying bone and marrow are necrotic, and the intact articular cortex and basal zone of the necrotic cartilage over not yet revascularized areas are dead.

The apposing acetabular cartilage (Fig. 6, d) shows basophilic staining of the midzone, tearing, and fibrillation. There is fibrous tissue proliferation of the subchondral bone, and articular fibrous tissue invasion of the cartilage which is undergoing ossification. The cartilage appears to be alive, but shows degenerative and reparative changes similar to those seen in senescent adult cartilage.

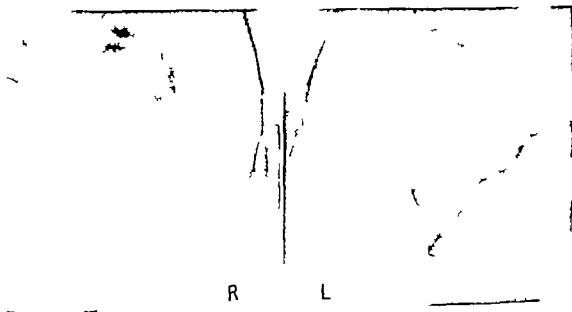


Fig. 4. Case Nonunion following separation of the right capital epiphysis. There has been moderate displacement of the left epiphysis followed by healing. Note the

reduced density and absorption of the cortex of the revascularized areas of the inferior third and superior margin of the necrotic right epiphysis.



Fig. 5. Case 2. Coronal section of the epiphyseal physis. Note revascularization of superior and inferior margins as well as the area about the fovea centralis.

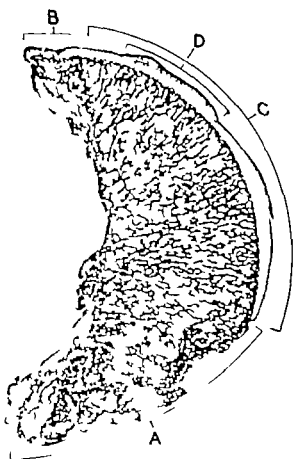


Fig. 6. Case 2. a, Photomicrograph of the epiphyseal physis, $\times 208$. b, Photomicrograph from articular surface showing fibrocartilaginous replacement of necrotic tissue above and absorption of articular cartilage below. $\times 16$. c, Photomicrograph of the articular surface showing fibrocartilaginous replacement of necrotic tissue by pannus overgrowth. $\times 38$. d, Photomicrograph of the articular surface showing changes in the apposing acetabular cartilage showing reactive changes. hematoxylin and eosin stain.



Fig. 6 b

Fig. 6 c

Fig. 6 d

The synovial membrane and capsul are thickened and fibrotic. The subintimal connective tissue is hyperplastic and hyalinized in many areas. There are scattered focal collections of lymphocytes and round cell infiltration about the smaller arterioles. No vessel showed obliteration of its lumen.

Extensive necrosis of the articular cartilage in both depth and surface area is seen in this specimen. The area of living cartilage (D Fig. 6 a) seems to be more resistant to absorption by pannus than the necrotic cartilage, and is thicker than the latter. The absorption of cartilage appears to have taken place more rapidly here it was exposed directly to the synovial membrane such as over the inferior third of the specimen. In this area, however, revascularization of the underlying bone undoubtedly contributed to the rapid absorption. Lack of weight bearing probably enhanced the overgrowth of pannus and superficial absorption of the cartilage over the contacting surface.

Following interruption of the blood supply to the epiphysis in adolescence the overlying articular cartilage may remain viable or undergo partial or complete necrosis. In either case subsequent degenerative or reparative changes apparently result in reduction of the depth of the articular cartilage as in the adult with aseptic necrosis of the head following fracture of the neck of the femur. This is in contrast to the changes seen in Legg Perthes disease where rapid growth of the living articular cartilage compensates for what ever absorption or ossification of the cartilage that takes place following revascularization of the ossification center. Under these circumstances, as mentioned previously, the depth of the articular cartilage usually increases.

The nonspecific chronic inflammatory changes in the synovial membrane appear to be due to irritation from the mechanical derangement of the joint. Such changes have been produced experimentally by Key and have been described in humans by Parker and associates following extensive stretching of the capsule associated with anatomical derangement of a joint. Irritation of the synovial membrane by decomposition products of the necrotic bone and cartilage may have been an additional factor in the production of the intense inflammatory reaction seen in the specimen from Case 1 of this report.

SUMMARY

Pathologic changes in the articular cartilage, ossification center and synovial membrane of 3 cases of aseptic necrosis of the capital femoral epiphysis following slipping of this epiphysis are described.

In Case 1 the bone of the epiphysis underwent necrosis but most of the articular cartilage remained alive. Bony union occurred, and at the end of one year about two thirds of the dead bone had been replaced by new bone. The articular cartilage was narrowed as its deeper zone had undergone degeneration and ossification, and growth of its superficial zone had been inadequate to preserve the normal depth of this structure.

In Case 2 there was nonunion and both ossification center and articular cartilage became necrotic. The necrotic articular cartilage underwent absorption and fibrocartilaginous replacement or ossification during the process of repair. Only a small amount of the necrotic bone had been absorbed and replaced by new bone.

The acetabular cartilage in one case appeared to remain viable. Early degenerative and reparative changes in this structure were noted.

The synovial membrane in both cases showed chronic nonspecific inflammatory changes.

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HODGKIN'S DISEASE OF THE BREAST

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IT is well over a century since Hodgkin described the disease of the lymphatic system which now bears his name. Since that time a large number of cases have been observed and a considerable body of factual data amassed, but much fundamental knowledge, particularly in the fields of etiology and treatment, is still lacking.

A noteworthy contribution to the understanding and treatment of this disease in recent years has been the recognition of primary types. Gilbert in 1939 stated that "primary" types include pulmonary and bony lesions with involvement of the peripheral nodes and lymphatic system. There is evidence that the disease in these cases is amenable to surgery in some locations. Craver has reported good results with this method in 11 cases in which the disease was confined to localized lymph node groups. Bini has reviewed the literature on primary gastrointestinal lymphogranuloma. The results in many of those patients treated by surgery are encouraging.

In the past few years Craver and his associates have studied the manifestations of the lymphatic system in different organs and organ systems and have reported the results of their investigations concerning osseous and pulmonary involvement. On the basis of these developments we decided to study breast involvement in Hodgkin's disease.

Hodgkin's disease is most uncommon as many writers have stressed. Symmers, for example, gives its incidence as 0.04 per cent of the approximately 50,000 annual admissions to Bellevue Hospital. An unusual manifestation of this disease is involvement of the breast. A review of the literature discloses only 8 reported cases, 5 of which are described in some detail, whereas the remainder are merely autopsy protocols. Kaufmann in his textbook of pathology gives no case report but states that the breast may be involved in generalized lymphogranulomatosis, and Goldman in an analysis of 212 cases mentions the finding of breast nodules in 4 of them.

During the period of 1932 to 1942, 406 patients with Hodgkin's disease were seen at the Memorial Hospital. Among this group there were 5 indi-

viduals or 1.25 per cent who exhibited specific breast lesions of Hodgkin's disease. Within the same time interval 3,901 cases of carcinoma of the breast were seen. A study of our patients with Hodgkin's disease of the breast as well as those reported in the literature reveals that with the exception of 1 woman aged 61, 63, and 67 years, respectively, the average age was 22.5 years. The tumor was situated in the right breast in 8 cases and in the left in 7 instances. There was 1 male and 4 females, and 1 negro, the latter fact being reported by Symmers and others have reported that the disease in this race is extremely rare. In a study of the reported cases of Hodgkin's disease of the breast, it is evident that it is itself as a primary condition or secondary to generalized lymphogranulomatosis. On this basis the following classification of primary carcinoma of the breast is proposed: (1) primary, (2) secondary including cases of lymphogranulomatosis.

In the literature may be considered 2 types of primary breast involvement and that of trigonum. In our own series 2 patients may be considered examples of this type. In one of these the history is that of the presence of a tumor in the breast for 1 year before the appearance of the axillary mass (Figs 1 and 2). Since no examination was made until both an axillary and breast mass were present, reliance must be placed on the patient's observation.

The other patient (Fig. 3) gave a history of a tumor in the right breast of 6 months duration. It was removed at another institution because it had become painful and was thought to be a lipoma. There were no other signs of the disease at the time of operation although axillary nodes appeared soon after. When the patient presented herself at our clinic there was inguinal, mediastinal and retroperitoneal disease.

Since the mode of spread of this disease is not well understood the condition may be considered primary in the breast only if there is no other evidence of the disease elsewhere in the body. For example, if the breast and corresponding axilla are involved there is no way of knowing which lesion antedated the other so that axillary disease unlike that associated with carcinoma is not nec-

From the Breast and Lymphoma Clinics of the Memorial Hospital, New York.



Fig. 1. The deformity produced by the metastatic outer portion of the right breast near the junction with the chest wall below the prominent axillary mass.

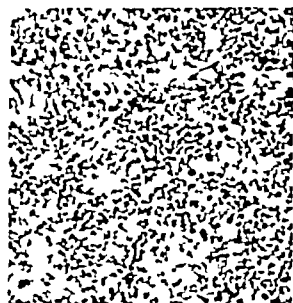


Fig. 2. Metastatic tumor of the breast. A cross-sectional view of the mass can be seen.

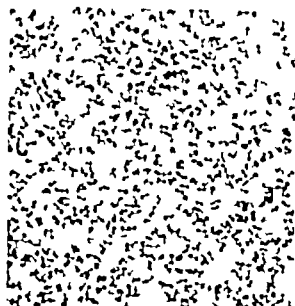


Fig. 3. Photomicrograph of breast tumor shown in previous photograph. Enlargement 75.

essarily secondary to the breast lesion. Even though there may be no evidence of the disease outside the breast the chest should be roentgenographed to eliminate the possibility of unsuspected mediastinal involvement.

A well-documented piece of evidence is accumulating which indicates that the expectation of life is increased in those cases of localized lymphatic granuloma treated surgically. Gail has recently analyzed a series of lymphoma subjected to surgery and found an increase in the life expectancy of those so handled when compared with those treated by other methods. Hence the importance of establishing a diagnosis of primary mammary lymphogranuloma lies in the fact that this malignant mass may be amenable to more treatment.

Histologically these tend to infiltrate the structures of the chest to the original lesion. Therefore, attention to this warning is imperative.

Secondary lymphatic masses have a tendency to infiltrate the tissues outside of the lymphatic system and just as often. Thus an entire breast and the peripheral tissues of the corresponding half of the thorax may become densely infiltrated. The case described by Kuecken, in which the intercostal and interlaminar muscles were involved, falls within this category. Taking these factors into consideration it would seem that radical mastectomy in all the cases might prove of value.

If the axillary nodes are involved the same procedure is certainly general and conservative.

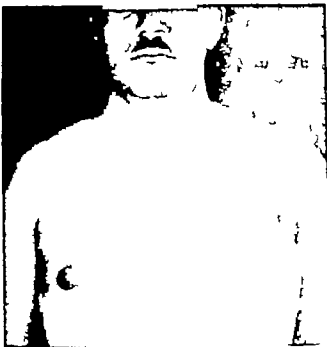


Fig. 4. The breasts are large. The dimpling of the skin above the right areola is well marked and mulberry-like as seen in carcinoma.



Fig. 5. Hodgkin's disease of the male breast. Photomicrograph (10x) of the dimpled area shown in preceding photograph (Fig. 4). Numerous Sternberg cells may be seen.

unsuitable for surgery. Symmers dictum in this connection is worthy of serious consideration. Writing on Hodgkin's disease he states:

"It is a subject of clinical value that enlargement of the axillary nodes is indicative of involvement of the cervical or thoracic groups, and that inguinal adenopathy in Hodgkin's disease presupposes involvement of the abdominal nodes. Enlargement of the axillary or inguinal nodes, independent of such associations, if it exists, was not recognized in the Bellevue Series."

In the total group of cases herein analyzed 5 were subjected to surgery. One of our patients had a local excision of the tumor and later developed generalized disease, whereas Wray's patient underwent an excision of the breast mass in the presence of generalized disease and died shortly thereafter. Another of our patients (Fig. 1) was treated by local excision of the breast lesion and an axillary dissection. She subsequently developed generalized disease. The patient of Kueckens and that of Risak and Kreibitz underwent radical mastectomy. In the former the disease was so extensive at the time of operation involving the opposite breast, that this individual in all probability was not materially benefited by the procedure. Risak's patient had ipsilateral axillary node involvement at the time of operation and subsequently developed a mass in the remaining breast and nodes in the corresponding axilla.

Of the 4 examples of primary breast involvement in this collected series only 3 were followed

until death and the last 2 were from our clinic. The average duration of life after the onset of the disease in these 3 patients was 4 years and 1 month. In the cases of secondary discrete involvement in our series the life duration of the patients after the initial appearance of disease was 4 years 2 months and 6 years 9 months respectively, an average of 5 years and 5 months. The life expectancy in Hodgkin's disease according to numerous authors is about 2 years and 8 months. Thus it is seen that in the cases we are discussing there was a definite increase in the life expectancy of the individuals with either primary or secondary breast involvement.

Although one cannot draw accurate conclusions from such a limited number of examples, nevertheless it may be that there is an increased life expectation in those cases that develop breast lesions. In primary involvement the explanation for this relative longevity may be that the disease remains localized in the breast for a considerable period before it appears in other locations. If that be true early diagnosis and surgical treatment may increase the expectation of life.

In the instances of secondary disease the explanation may be that the involvement of the breast under these circumstances is a late manifestation which occurs in the relatively long-lived cases. In this it may be comparable to the abdominal manifestations of Hodgkin's disease which we

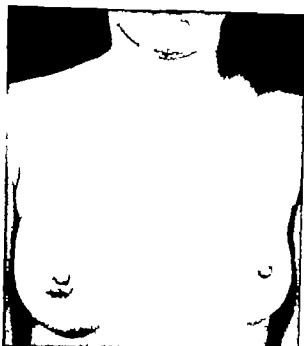


Fig. 6 The right breast is about half again the size of the left



Fig. 7 Aspiration biopsy specimen of the enlarged breast depicted in the preceding photograph (Fig. 6) showing the sarcomatous nature of the breast involvement. X60.

have found to be a development late in the course of the disease and a phenomenon occurring in those patients with relative longevity.

There are 2 examples of secondary breast involvement in our series. The first case, a male, is depicted in Figure 4. The dimpling of the skin over the mass is well developed and simulates that seen in carcinoma. The mass in the breast appeared 3 years, 5 months after the onset of the disease. It regressed somewhat with radiation but subsequently broke down and formed an ulcer which was ultimately excised. Figure 5 is a photomicrograph of tissue from the excised ulcerated area. Numerous characteristic Sternberg cells may be seen.

In the other case of secondary breast involvement the lump appeared in the breast 2 years and 2 months after the onset of the disease. Although the aspiration biopsy of this mass was unsatisfactory, it seems reasonable to conclude that this was a specific lesion because of its response to irradiation. With high voltage roentgen irradiation the mass regressed to one half of its original size.

The diffuse type of secondary breast involvement as exemplified by one of our patients is a strange phenomenon. The breast becomes diffusely enlarged and thickened with infiltration and edema of the skin (Fig. 6). The aspiration biopsy of this breast (Fig. 7) reveals the sarcomatous nature of the involvement. In this case the process appeared to be fulminating, the patient dying 9 months after the onset of the disease and 1 month after the involvement of the breast. There may be an analogy between inflammatory carcinoma of the breast in which the subcutaneous lymph spaces become engorged with cancer cells,

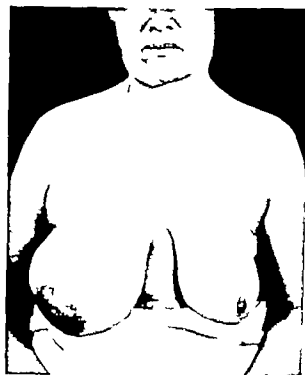


Fig. 8 The enlargement of the right breast and appearance of *pseudo-Sternberg* cells demonstrated as well as the right axillary mass. There are discoloration and marks from scratching over the anterior chest wall and upper aspect of the breasts.

and the diffuse type of Hodgkin's involvement in which the phenomenon may be caused by the engorgement of the subcutaneous lymphatics with lymphomatous cells.

In Gendreau's patient the condition appeared as a primary process, the left breast gradually enlarging until it was about three times its normal size. However, since there was no positive biopsy of the breast obtained at any time it cannot be regarded with certainty as an example of diffuse involvement by Hodgkin's disease. The enlargement may have been produced by lymph stasis secondary to pressure on the lymphatics by enlarged nodes.

We had a case similar in some respects to the foregoing one.

This was a 42 year old white woman who came to the clinic complaining of a painless enlarged right breast of 1 year's duration during which time it had increased to about two and one half times its original size. For 6 years preceding this episode she had received x-ray therapy at intervals for enlarged right lower cervical nodes. They decreased in size after each series of treatments but soon thereafter began slowly to enlarge. Shortly before the onset of the breast enlargement she noticed a painless swelling of the right axilla. Later the left cervical nodes increased in size. During this year she suffered from generalized pruritus.

Examination revealed marked enlargement of the supraclavicular anterior and posterior cervical nodes. They were firm discrete, and varied in size from that of a pea to 4 centimeters in diameter. In the right axilla was one large node measuring 9 centimeters in diameter and several smaller ones. There were several shotty nodes palpable in each groin.

The right breast was considerably enlarged with *peau d'orange* appearance of two-thirds of the skin, marked lymphedema and slight nipple retraction (Fig. 8). The entire breast had a firm, indurated consistency. The left breast exhibited a small area of *peau d'orange* with a minimal amount of lymphedema. The skin over the chest was excoriated from scratching.

X-ray examination of the thorax revealed evidence of a large quantity of right sided pleural fluid and widening of the upper mediastinum. Blood examination showed hemoglobin, 90; red blood count, 4.6; white blood count, 13,400; polymorphonuclears, 76; large lymphocytes, 1; small lymphocytes, 20; mononuclears 3; eosinophils, 1.

The clinical diagnosis was Hodgkin's disease but it was not verified because the patient refused biopsy. After receiving a small amount of x-ray therapy she failed to return and was lost to follow up. The breast enlargement in this case we believe is attributable to lymph stasis secondary to mechanical obstruction produced by enlarged lymph nodes. It is possible, however, that it might have been caused by lymphomatous infiltration of the breast in a manner similar to that of the foregoing case.

Another example of this same phenomenon was seen by us.

This was in a girl whose illness began at the age of 20 with enlargement of the lymph nodes in the left side of the neck. One of these nodes was examined by biopsy and the report was Hodgkin's disease.

There was slow progression of the disease over a period of about 5 years during which time she developed nodes in the axillae more marked in the right, and disease in the lungs. About this time, 5 years after the onset of the disease, she began to notice a painless, progressive enlargement of the right breast which continued for about 3 months. Examination at this time revealed the right breast to be 50 per cent larger than the left but there was no change in its consistency when compared with the left. There were many large nodes in the right axilla forming a 3 by 4 centimeter mass. X-ray examination of the chest revealed a large quantity of pleural fluid on the right side. Previous films had shown mediastinal widening.

She received high voltage x-ray therapy to the right axilla and mediastinum with subsidence of the breast enlargement and disappearance of the axillary nodes and the pleural effusion. A check-up 6 months later revealed no evidence of disease. This patient lived 8 years longer, a total of 3 years from the onset of the disease during which time she had recurrences of lymph node and pulmonary manifestations controlled by x-ray therapy. Ultimately she died from the disease.

The breast enlargement in this instance may have been due to lymph stasis produced by enlarged axillary and mediastinal nodes. The disappearance of these node masses with radiation therapy and the consequent establishment of normal lymph drainage may have been responsible for the return of the breast to normal size. On the other hand, if the enlargement was due to disease infiltration the subsidence may have been produced by some of the radiation which was directed to the axilla and mediastinum reaching the breast itself.

An enlargement of the breast secondary to axillary involvement but with a different underlying mechanism was reported by Middleton. In his patient a 58 year old white woman, the disease began in the right axilla as a node which in the course of 6 months, enlarged downward and forward into the breast and posteriorly over the latissimus dorsi. It did not, however, involve the apex of the axilla and there was no other lymphadenopathy. The mass in the right axilla was resected and reported as 'Hodgkin's disease'.

Another rather unusual case of breast enlargement occurring in the course of Hodgkin's disease is the following.

The patient, a 48 year old white woman, consulted her physician because of a tender area in the left axilla. At the time of examination she had a nodule the size of a hickory nut in this axilla and a pyrexia of 101 degrees F. The breasts were entirely normal. A blood count was normal and an x-ray film of the chest was negative. The mass in the axilla was excised at another institution and was diagnosed as lymphosarcoma. The specimen was then submitted to Dr. Fred Stewart whose report was as follows: "Not typical lymphosarcoma. Partial obliteration of normal architecture. Diffuse overgrowth of small lymphocytes. Rare

cation, melena and loss of weight. The pregnancy was of 4 months duration. A colostomy was performed. Three weeks later the coccyx, the last segment of the sacrum, and the entire rectum and anus, together with the greater part of the levator ani muscle were removed. The lesion was a columnar cell carcinoma which weighed 63½ pounds (29 kgm.) In the 2d case the patient was a 38 year old decigravida, nonipara, who was in the 3d month of pregnancy. She complained of chronic constipation and a bloody mucous rectal discharge. A colostomy was followed by a combined abdominoperineal resection (Kraske type). The pathologic diagnosis was columnar cell carcinoma of the rectum. Spontaneous labor occurred 6 months after the operation. The author expressed the opinion that the two stage operation was easier and less dangerous than a single stage procedure.

Fairbairn in 1927 reported a case of persistent vomiting of pregnancy. The patient was in the 8th month of pregnancy. After termination of the pregnancy an operation was performed for carcinoma of the colon which had become obvious after the uterus was emptied. No data were reported regarding the subsequent condition of the patient. In the same year Mussey and Crane reported several cases in which operations had to be performed on pregnant women. Among them was a case in which carcinoma of the rectum was removed by a posterior resection of the rectum after a preliminary colostomy. The patient was in the 5th month of pregnancy. The infant subsequently was delivered by cesarean section. Mengert in 1933 reported that he had performed a cesarean section on a woman who had an adenocarcinoma of the sigmoid colon that had perforated and who also had decompensated heart disease. In 1936 Mikale reported a case in which abortion was induced because of an annular carcinoma of the terminal part of the ileum. The author believed that the existence of partial or intermittent intestinal occlusion should be strongly considered whenever the symptoms commonly associated with a normal pregnancy become exaggerated. In 1936 Pommerenke reported the recovery of 2 parturient women after abdominoperineal resection of the rectum. The first patient consulted her physician because of bloody mucous stools, constipation, and loss of weight. A diagnosis of adenocarcinoma of the rectum was made and a one stage abdominoperineal resection was performed. When the patient was seen in the prenatal clinic 19 months after the operation, she was in the 7th month of pregnancy. Delivery at term was uneventful. Shortly thereafter she

again became pregnant and again delivery was uneventful. The author remarked regarding the "easy labor" noted. He attributed this to decreased perineal resistance. He expressed the opinion that the female generative organs may well be preserved intact at the time of radical operation which proves that the reproductive function is not affected. Ducuing in 1939 reported a case in which pregnancy was associated with an inoperable carcinoma that had caused a rectovaginal fistula. The patient was a woman, 31 years of age. She consulted her physician during the 7th month of gestation. A Porro cesarean section was performed and a living baby weighing 2800 grams was delivered. The mother was subsequently treated with radium and at the time the article was written both mother and child were alive. Adair in 1940 recommended the interruption of pregnancy as soon as possible after a diagnosis of carcinoma is made provided that this procedure offers a possibility of cure. He said that occasionally the malignant lesion spreads more rapidly during pregnancy. This has not been substantiated by the work of Maude Slye on rats which suggests a retardation of tumor growth in general during pregnancy especially when there has been no interval between pregnancies.

In 1940 DerBrucke reported a case in which intestinal obstruction was due to a malignant lesion complicating pregnancy. He also noticed the similarity of symptoms found in cases of intestinal obstruction and those commonly found in pregnancy. He spoke principally regarding constipation, distention, vomiting and pain. He believed only 5 authenticated reports of carcinoma of the large bowel during pregnancy had appeared in the literature prior to 1940 and he added 2 cases. In the first case the patient was a primigravida who complained of distention, constipation, and vomiting accompanied by pain and tenderness over the sigmoid region. She was in the 8th month of pregnancy. Induction of labor resulted in a living infant but the mother died after a subsequent operation. The pathologic diagnosis was adenocarcinoma of the intestine, fallopian tubes, ovary and pelvic tissues. In the 2d case the patient was a 36 year old tertigravida secundipara, who at the 6th month of pregnancy complained of vomiting, distention, and constipation which had been present for 1 week. An exploratory laparotomy was performed and specimens of the omentum were removed for biopsy which revealed carcinoma. After abortion had occurred the patient died of metastatic adenocarcinoma. The author expressed the opinion

that drastic purging is dangerous in cases of prolonged constipation and that the diagnosis of neoplasm of the intestine especially in cases in which intestinal obstruction is present can be made easily by roentgenologic examination. Der Brucke stated that a malignant lesion apparently has little effect on pregnancy. If a diagnosis of a malignant lesion is made in the early months of pregnancy the pregnancy should be disregarded and the neoplasm treated in the usual manner. If the diagnosis is not made until after viability of the fetus, the fetus should be delivered from below and laparotomy should be performed immediately thereafter.

In 1941 Mayo and one of us (A.B.H.) reported a case in which carcinoma of the rectum complicated pregnancy. In this case a subsacral resection was performed and the anus was preserved.

Up until 1943 there have appeared in the literature a total of 62 cases in which carcinoma of the intestine has complicated pregnancy. The diagnosis was not confirmed by microscopic examination in all of these cases. The maternal mortality which was recorded in 41 of the 62 cases was 63 per cent. The fetal mortality which was recorded in 40 of the 62 cases was 50 per cent.

REPORT OF CASES

CASE 1. A 39 year old woman, secundigravida, primipara, had had abdominal cramps, nausea, vomiting and abdominal pain for approximately 1 month before she came to the clinic. The patient was well developed but moderately dehydrated. The size of the uterus indicated a pregnancy of about 5 months but no fetal heart tones could be heard. Roentgenologic examination revealed a polypoid growth of the transverse colon. Because of associated anemia, 500 cubic centimeters of citrated blood was transfused. An exteriorization operation was performed with clamps. The immediate postoperative course was uneventful. Progesterone was administered in doses of 2.5 milligrams daily and adequate sedation was employed. The patient left the hospital on the 14th day after the operation. Microscopic examination disclosed an adenocarcinoma which was graded 3 according to the method of Broders and classified as type B according to the method of Dukes. Two months after the operation the patient returned to the clinic and a colonic stoma was closed satisfactorily. Four months postoperatively a normal male infant was delivered through the pelvis.

CASE 2. A 38 year old woman, sextigravida, tertipara, was referred to the clinic because of rectal bleeding and abdominal cramps of 8 months' duration. She was in the 7th month of pregnancy. Proctoscopic examination revealed an ulcerative lesion with fixation, grade 3 and obstruction, grade 4, 14 centimeters above the anus. Biopsy disclosed that the lesion was an adenocarcinoma, grade 3. Anterior resection of the sigmoid colon was performed and a single barrelled permanent colonic stoma was established. The growth was situated just above the rectosigmoid and too low to be removed by extraperitoneal resection. The immediate postoperative convalescence was uneventful however on the 4th day after operation the woman gave birth to an infant weighing 700 grams. In

spite of 3 blood transfusions, administration of oxygen and sulfonamide drugs, and the use of various supportive measures, the patient died on the 6th day after the operation. The infant died a few hours after birth.

CASE 3. A patient, 42 years of age, was referred to the clinic because of intermittent rectal bleeding and diarrhea which had been present for approximately 2 years. Proctoscopic examination revealed a lesion 8 centimeters above the anus and biopsy disclosed that it was an adenocarcinoma, grade 2. The patient apparently was in about the 5th month of pregnancy. Subacral resection with an end-to-end anastomosis was performed and the lesion was removed. The lesion was classified as type B according to the method of Dukes. Postoperatively the patient received a blood transfusion, progesterone, and sulfonamide therapy. She was dismissed from the hospital on the 16th day after the operation. She returned to the clinic in the 38th week of pregnancy and a normal male infant was delivered by low cervical cesarean section. Exploration of the abdomen at this time did not disclose any abnormality and the results of proctoscopic examination also were negative.

CASE 4. A woman, 30 years of age, was referred to the clinic because of rectal bleeding, abdominal cramps, alternating diarrhea and constipation and loss of weight which had been present for 1 year. She was in the 5th month of pregnancy. Proctoscopic and roentgenologic examination revealed a growth in the rectum. Biopsy disclosed that the lesion was an adenocarcinoma, grade 3. Through a left rectus incision, a Littlewood Maydl type of colostomy was performed. This was followed by a posterior resection of the rectum and 3 inches (5.08 cm.) of the sigmoid colon. The cecum and 5th sacral vertebra also were removed. The patient made an uneventful recovery and was dismissed from the hospital on the 30th day after the operation. The adenocarcinoma was classified as type C according to the method of Dukes. Five months later a normal infant was delivered by a Porro-cesarean section. Exploration of the pelvis revealed no further evidence of the growth.

CASE 5. A 29 year old woman, tertigravida, secundipara, was referred to the clinic because of bloody stools, cramps, and alternating diarrhea and constipation which had been present for 1 year. The physical findings revealed nothing of significance. Roentgenologic examination revealed a polypoid lesion of the rectosigmoid. A permanent colostomy (Mixer type) was performed. This was followed by a Kraake resection. Examination of the specimen revealed an adenocarcinoma which was graded 3 according to the method of Broders and classified as type B according to the method of Dukes. The patient made an uneventful recovery from the operation. Four years later she returned to the clinic because of amenorrhea. She was found to be pregnant and advised to permit the pregnancy to continue until approximately the 38th week. At this time a classic cesarean section was performed and the patient was sterilized. Abdominal exploration revealed no further evidence of the growth. The postoperative course was uneventful.

CASE 6. A 28 year old woman, who was in the 8th month of pregnancy was referred to the clinic because of rectal bleeding and tenesmus. Proctoscopic examination revealed a rectal polyp which, when removed, was found to be carcinomatous. The course of the pregnancy and the subsequent delivery were uneventful.

CASE 7. A 34 year old woman was referred to the clinic because of abdominal discomfort of 1 year's duration. She was a tertigravida and tertipara. Proctoscopic and roentgenologic examination revealed a polypoid tumor of the second portion of the descending colon and microscopic examination revealed that the tumor was an adenocarcinoma, grade 3. An exteriorization operation was performed. The tumor was graded 3 according to the method of Broders

nal outcome was known. The gross fetal mortality was 50 per cent in cases in which surgical treatment was employed. This report adds 7 additional cases of pregnancy associated with carcinoma of the large bowel. The maternal mortality and the corrected fetal mortality were both 14.3 per cent in these 7 cases.

The age and weight of the patients as well as the concentration of hemoglobin in the blood and the sedimentation rate of the erythrocytes are of little value in arriving at a diagnosis of carcinoma of the intestinal tract in pregnancy. Some symptoms of carcinoma of the colon or rectum, such as nausea, vomiting and constipation, are thought to be commonly associated with pregnancy. Proctoscopic and roentgenologic examination of the colon should be performed in all cases in which pregnant women complain of unexplained constipation, diarrhea, or bloody discharge from the lower part of the bowel. Nausea and vomiting especially in the latter half of pregnancy demand the exclusion of carcinoma of the colon.

An attempt has been made to outline rational methods of both surgical treatment of the carcinoma and management of parturition in cases in which carcinoma of the large bowel is associated with pregnancy. On reviewing the literature one is impressed by the ease with which delivery takes

place through the pelvis even after removal of the lower part of the sigmoid colon and rectum.

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ARTERIOVENOUS ANEURYSM

IT is already apparent that in this war the incidence of vascular injuries will surpass that of any other war. Multiple wounds the result of fragmentation of land mines, high explosive shells, and grenades increase the chance of blood vessel damage since as many as one hundred wounds capable of producing such an injury are frequently seen in a single individual without producing death. Moreover, improved methods for the control of shock and infection and the early medical care and rapid evacuation of the wounded have preserved a greater number for subsequent observation.

In accordance with the program of the Surgeon General, certain general hospitals have been designated for specialized treatment, and a Vascular Surgery Center was established in January 1943 (Ashford General Hospital). Lately two other such centers (DeWitt General Hospital and Percy Jones General Hospital) have been established.

The most common lesion resulting from direct injury to blood vessels has been the

establishment of an arteriovenous fistula. This may be produced by the smallest of fragments just as in civilian life they have been noted following knife and ice pick wounds. The application of skeletal fixation pins, injury from transfexion sutures or by the accidental injury of arteries and veins in performing venotomy. Since the fistulas may be small and symptomless in the early stages they are often overlooked both in civil and military practice unless careful examination of every wound is carried out. A small missile may produce an external injury so slight as to be regarded as of little importance but at the same time produce extensive damage to the underlying artery and vein.

Frequently patients are erroneously treated for varicose veins and ulcers when an arteriovenous aneurysm responsible for this condition through preventing proper nourishment of the part is the cause. Moreover, signs of cardiac failure may supervene before its real cause is discovered. Inconspicuous wounds or those in which the main injury involved nerve, bone, or soft tissues may also involve blood vessels which are frequently overlooked through failure of the examiner to suspect their presence or because his attention has been diverted to a seemingly more important lesion. It must be borne in mind that the presence of one fistula does not preclude the presence of one or more elsewhere in the same individual. Several patients have been observed with two fistulas and in one three were present.

The differentiation of a false aneurysm and an arteriovenous fistula is important since the sequelae, the general and local effects as well as the treatment, are altogether different. The

differential diagnosis is not always easy but as a rule the *arteriovenous aneurysm* is characterized by a *continuous* vibratory thrill and a loud, rough continuous murmur with systolic intensification whereas in the false aneurysm there is distinct pause between the systolic and diastolic phases and often the murmur is heard only in systole. In an *arteriovenous communication* the murmur is usually transmitted for some distance on either side along the course of the vessels whereas in an aneurysm confined to an artery the murmur is rarely heard beyond the confines of the dilatation.

Certain general and local effects follow the establishment of an *arteriovenous fistula*. These are dependent upon the size of the opening, the vessel involved, and the duration of the lesion. Early signs vary. The extent of initial external bleeding is variable and can usually be controlled by pressure although in some instances ligation is necessary. After an interval of time the patient may discover the thrill so characteristic of this condition. In other instances it may be found only after careful examination.

Establishment of a fistula introduces a secondary circuit into the vascular system. The peripheral resistance in this circuit is lowered, the capillary barrier being eliminated, and arterial blood is short-circuited directly from artery to vein. In a fistula of a large vessel, like the femoral, one-fifth to one-half of the blood ejected by the left ventricle is shunted to the right side. If the fistula is sufficiently large enough blood may be diverted into the venous system proximal and distal to the fistula, to produce a general drop in blood pressure and even death. In more instances, the blood pressure changes are not extreme, the systolic pressure soon returns to normal, but the diastolic pressure as a reflection of the general lowering of peripheral resistance re-

mains lowered. The effect on the blood pressure is similar to that seen in aortic insufficiency although there the leak is into the left ventricle and here into the venous system. Increased venous pressure in the circuit proximal to the fistula reflects the increased venous filling. The heart accommodates to the increased venous return by acceleration of rate and increased strength of contraction effecting an increase in cardiac output. Soon an increased circulating blood volume is added as another compensatory mechanism.

The normal heart usually can tolerate the increased demands made upon it but as the leak in the circulation persists and actually becomes greater as the fistula increases in size, difficulties appear. The heart begins to dilate and circulatory symptoms appear. Dilatation and later hypertrophy result from the increased work the heart is called upon to perform and circulatory failure may supervene. The artery proximal to the fistula also dilates, and the dilatation may extend as far back as the heart itself. This may be due to the greatly increased blood mass in the shorter circuit due to the decreased resistance at the site of the fistula as suggested by Holman.

The immediate effect of temporary occlusion of the fistula is redistribution of the circulating blood volume. Blood no longer flows freely through the opening into the venous system and temporarily overfills the general circulation. The blood pressure rises and the heart may distend. Reflexly via the carotid sinus the heart is slowed (Branham's sign) and some peripheral dilatation occurs. Usually a temporary rise in systolic and diastolic pressures occurs. With excision of the fistula, the diastolic pressure returns to normal levels, and the systolic pressure rising temporarily soon returns to normal. There may be a temporary increase in size of an already dilated heart, but with return of blood volume

to normal (often after several days) the heart returns to its normal size unless irreparable myocardial damage has taken place

There is no condition which produces such an extensive collateral circulation as does the interposition of a fistula between an artery and a vein. However this circulation is for the most part useless since most of the blood in the collateral vessels passes back through the fistula without reaching the part beyond it. While this circulation is of little value when the fistula is open it means that an operation for its elimination can be carried out without fear of resulting gangrene provided sufficient time is allowed for full development of collaterals.

The effect on the heart as well as the local effects demand that an arteriovenous fistula be eliminated. Time allowed for development of collateral circulation (two or three months) should not be prolonged until pronounced cardiac damage has occurred or nutrition of the part involved is affected. *Mere ligation of*

major vessels will not cure the lesion and more often leads to gangrene of a limb. On theoretic grounds it would seem best to repair the opening in the artery and vein and at the same time maintain their continuity. Such a procedure is technically difficult and frequently results in secondary hemorrhage or recurrence of the lesion. Since the collateral circulation is of such abundance quadruple ligation of the proximal and distal arteries and veins and *complete excision of the fistula is the method of choice*. Where technical difficulties preclude this procedure the fistula may be eliminated by ligation and division of the main vessels followed by closure of the communication through the opened vein by the passage of mass ligatures about the area of the fistula or by separation of the vessels and closure of the opening in each. Nutrition of the area distal to the fistula will immediately improve since the blood formerly diverted will reach the part through the collateral vessels.

DANIEL C. ELKIN

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REVIEWS OF NEW BOOKS

THE most complete book that has yet appeared concerning experiences in the treatment of facial injuries in this war has been written by Fry and his co-authors. He is consulting dental surgeon to the Royal Air Force and all of the authors are associated with Mr. A. H. McIndoe at the East Grinstead Maxillo-facial Unit.

There are very good chapters on the anatomical considerations, causes and types of fractures, diagnosis, radiological interpretation, associated injuries, pathology of bone and soft tissue repair and reduction and fixation of fractures as well as the technique of making the splints and apparatus required. An other interesting section concerns the recommended field and preliminary hospital treatment based upon their recent experiences and there is an excellent chapter on fractures of the middle third of the face written by Mr. McIndoe.

The authors divide jaw fractures into four general types (a) *cranial* type fractures which are usually indirect, caused by minor accidents (falls, blows, kicks etc.) and are characterized by relatively little displacement, comminution, or loss of bone (b) *crush* injuries, resulting from accidents in mechanized equipment and airplanes, which are characterized by a multiplicity of fractures, both indirect and direct and in which loss of bone and comminution is uncommon though there may be extensive soft tissue injury as well as associated shock and skull fractures (c) *gunshot* injuries which are direct and characterized by gross comminution, loss of bone and extensive loss of soft tissue at the exit though the patient's general condition is usually good, few suffering from much shock (d) *air raid* injuries which may be crush or gunshot in character but are often accompanied by profound shock as a result of the blast and often have dirt of all kinds driven deeply into the skin and soft tissues. Their description of the various types of injuries encountered in this war is lucid and interesting, and the methods of treatment employed are well described and illustrated.

The book is written in a concise, straightforward manner and brings out the complications and difficult situations which may be encountered, together with the various forms of management which have been used. The authors are somewhat more enthusiastic about the use of cast splints than many workers in this country but perhaps we should at least

re-examine our attitude toward them. The book is recommended to all who are interested in the care of these injuries.

FR. W. McDOWELL.

THE amount of study and review which forms the basis of the monograph *Hydronephrosis and Pyelitis of Pregnancy* by Robertson is overwhelming in its magnitude. Nine hundred seventy-four contributions on all phases of the subject are used as the author's background to add to his personal experience. It is surely a most comprehensive analysis of all that is known about the urinary tract complications which are associated with pregnancy.

The physiology, pathology, diagnostic complications and residual effects of the hydronephrosis, both noninfected and infected which accompany the pregnant state are discussed in the greatest detail from the point of view of etiology and pathogenesis.

In Robertson's hands this subject embraces the many closely related phases such as albuminuria, eclampsia, the so called kidney of pregnancy and the complications of childbirth and the puerperium. The rôle of vitamin deficiency and the possible hormonal effects of pregnancy are carefully considered. This work together with the one of Crabtree on *Urologic Diseases of Pregnancy* should constitute a complete library for anatomists, bacteriologists, obstetricians, gynecologists, urologists and roentgenologists as an all-embracing source of knowledge and reference.

VICTOR J. O'CONNOR.

WITH the flood of new methods propounded during the past few years for the diagnosis and treatment of neurosurgical conditions, it is remarkable that a young author should be able to write a book dealing with those matters with such effective simplicity and adherence to sound clinical fundamentals as has Dr. Rand in his book *The Neurosurgical Patient*. Here is a discussion of some 54 neurosurgical subjects, each handled directly, simply, logically, and with a wise avoidance of controversial matters and current disagreement about neurosurgical treatment.

The author has made it plain that he does not consider the book a compendium of knowledge on the subject of neurosurgical surgery. He has written a practical treatise for the student and general practitioner but at the same time he has presented much sound material which would serve as a valuable review and information for any neurosurgical surgeon.

HYDRONEPHROSIS AND PYELITIS (PYELOPHLEBITIS) OF PREGNANCY. ENDOCRINE AND PATHOLOGICAL HISTORICAL REVIEW By H. C. Robertson, M.D. Philadelphia and London. W. B. Saunders Co. 1944.

THE NEUROSURGICAL PATIENT By Carl W. Rand, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1944.

THE DENTAL TREATMENT OF MAXILLO-FACIAL LESIONS WITH SPECIAL REFERENCE TO TRAUMA OF THE FACE By W. Kelsey Fry M.C., M.R.C.S., L.R.C.P., L.D.S., R.C.S., F. Rae Shepherd, F.R.C.S., Alan C. McIndoe, D.D.S., B.Sc., L.D.S., R.C.S., and Gilbert J. Parfitt, M.R.C.A., L.R.C.P., L.D.S., R.C.S. Philadelphia and Montreal: J. B. Lippincott Co. 1944.

The material is presented in a novel manner being written as a series of reports of clinics held for students, wherein patients are presented for a review of their histories and for physical examination. Superfluous discussion, long references to old literature and topics requiring lengthy and tiresome review are avoided as they necessarily would be in a regularly scheduled student clinic. The style is easy, sometimes downright conversational, always friendly, yet with such a treatment the dignified subject is never handled without dignity. Such an author could only be an honest diagnostician and a kindly practical philosopher.

Not everyone will agree that sawdust would make a convenient bed for paralyzed patients with spinal cord injuries. Many present-day enthusiasts for early activation of patients with head injury will not agree with the author's conservatism in keeping such patients in bed for a safely long period of time. Some neurological surgeons will feel that he has not devoted sufficient space to the diagnosis and treatment of peripheral nerve injuries (30 pages in a 576-page book). The language purist may at times be annoyed by some of the rather loose conversational sentence structure. The illustrations are not profuse, but some of those shown are superb. Figure 103 is an unusual illustration of an air-filled cavity of the septum pellucidum. References for collateral reading are pertinent and modern.

Dr Rand's book is sound and enjoyable reading. It is one that can be read and understood by students, and it will no doubt find its way into the third and fourth year curriculum of more than one medical school.

JOHN MARTIN

IN recent years the standard American text of surgery of the eye has been Edmund Spaeth's *Principles and Practice of Ophthalmic Surgery*.¹ In the third edition the outline of the text is the same as that in the previous editions, a chapter on anesthesia introduces the book and is followed by chapters on the orbit, lacrimal apparatus, extraocular muscles, reconstructive plastic surgery, surgery of the lids, conjunctiva, cornea and sclera, iris, intraocular procedures, and the book concludes with a chapter on irradiation.

Over one hundred new illustrations and diagrams have been added. They are uniformly excellent and contrast rather sharply with some of the old ones which would have been better deleted. The section on muscles now includes a discussion of the physiology of squint. The section on ptosis has been rewritten and a useful classification with the proper surgical considerations of each type is presented. The author has devoted more discussion to injuries of the globe, lids and orbit. Irradiation of tumors and the plastic repair of tumor sites are subjects which now properly occupy a separate concise section of the book which is one of the most valuable additions to the revised edition.

THE PRINCIPLES AND PRACTICE OF OPHTHALMIC SURGERY. By Edmund B. Spaeth, M.D. 3d ed. Philadelphia: Lea & Febiger, 1944.

As in the previous editions numerous authorities are quoted verbatim, particularly Walker and Stalard in the fields of retinal detachment and radium therapy. Castroviejo has contributed the section on corneal transplantation and Otto Barkan the section on goniotomy.

The discussions of the indications, contraindications and complications of the various antiglaucoma procedures and of cataract extraction should be read by every ophthalmic surgeon.

This text should continue to enjoy all the popularity it has had in the past.

DEAN SPEAR.

PROGRESS in urology during the past five years has made it necessary completely to review many of the descriptions of pathology and treatment. Lowley and Kirwin² have thoroughly revised their comprehensive textbook on the nature, diagnosis and treatment of the anomalies and diseases of the genitourinary organs. All of the old subjects have been brought up to date and many new subjects have been added. These two volumes are quite outstanding as guides in the practice of clinical urology and will appeal to specialist and general practitioner as an ideal reference work. The subject matter is very complete and is clearly outlined. The readability of the type and the attractive compilation of the text add greatly to the value of the work. The splendid illustrations of William P. Didusch represent the result of many years of devoted talent to this particular subject. Lowley and Kirwin are to be commended for this thoroughly revised edition which includes the many recent medical and surgical additions to urological knowledge and practice.

VINCENT J. O'CONNOR.

AS Dr. Bierman is in charge of the Department of Physical Medicine at the New York University Medical College which received a large grant from the Baruch Committee on Physical Medicine and also is in charge of the Department of Physical Medicine at a large hospital, he is well qualified to write a book such as *Physical Medicine in General Practice*.³

The author states that this book is written for the general practitioner as well as those in special fields to tell how physical measures can be employed. Historical references and extensive descriptions of the physics of light, heat and electricity are omitted but the techniques of the application of physical measures and their physiologic rationale are emphasized. At the end of each chapter an excellent bibliography is given for reference.

Bierman emphasizes that physical therapy has its limitations and also has the potentiality for doing harm. The pitfalls which should be avoided are discussed in an excellent chapter on the conduct of treatments. For the general information of the

SCIENTIFIC UROLOGY. By Os. W. S. Lowley, A.B. M.D. FACS and Thomas J. Kirwin, M.A. M.B. M.D. FACS. 1st and 2d ed. Baltimore: The Williams & Wilkins Co., 1944.
PHYSICAL MEDICINE. GENERAL PRACTICE. By William Bierman, M.D. New York: P. B. Hoeber, Inc., 1944.

tuberculosis. He has included well selected fundamental work from the recent literature which has not as yet appeared in book form. For this reason his volume is as up to date as any that appear. In

addition the book is very nicely assembled, has good illustrations and a very readable text. I believe it is a worthwhile addition to the literature on the subject.

JOHN M. DUNN

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

METHODS OF ANATOMY DESCRIPTIVE AND DISSECTIVE. By J. C. Boyle, Grant, M.C., M.B. Ch.B. F.R.C.S. (Edin.). Baltimore: The Williams & Wilkins Co. 944.

THE ART OF RE-EXAMINATION. By Paul J. Flagg, M.D. New York: The Reinhold Publishing Co. 944.

FRACTURES AND FRACTURE TREATMENT IN PRACTICE. By Kurt Cohen, M.D. Johnsburg, Wittenberg University Press, 944.

THE BIOLOGY OF THE ORIGIN OF LIFE. By Leo Loeb, Springfield, Ill. and Baltimore, Md. Charles C. Thomas, 945.

INTER-SCIENTIFIC HANDBOOK. Directed by M. S. Dooley, A.B. M.D., and M. J. Holmes, M.D. F.A.C.P. Philadelphia, London, Montreal: J. B. Lippincott Co. 944.

AN OUTLINE OF TROPICAL MEDICINE. By Ott Saphi, M.D. Chicago: The Michael Reese Research Foundation, 944.

TREATMENT BY MANIPULATION IN GENERAL AND CONSULTING PRACTICE. By A. G. Timbrell Fisher, M.C. M.B. Ch.B. F.R.C.S. (Eng.). New York: Paul B. Hoeber Inc. 944.

LA DIRECCION GENERAL DE HIGIENE DE LA PROVINCIA DE BUENOS AIRES. By Dr. Juan Leon. Buenos Aires: El Ateneo, 944.

RECONSTRUCTION SURGERY. Edited by James Thomson, M.D. Ann Arbor, Michigan: Laid Brothers, Inc., 944.

MEDICAL DISEASES OF WAR. By Sir Arthur H. Hall, M.A., M.S. F.R.C.P. Baltimore: The Williams & Wilkins Co., 944.

AIDS TO ORTHOPEDIC SURGERY OF FRACTURES. By I. E. Zies, M.A., F.R.C.S. 2d ed. London: Baillière, Tindall, and Cox, 944.

THE WOMAN AS THE DOCTOR. By Louis Novak, M.D. F.A.C.S. 2d ed. Baltimore: The Williams & Wilkins Co. 944.

TRANSACTIONS OF THE SOUTH AFRICAN SURGICAL ASSOCIATION. Vol. 55. FIFTY-FIFTH ANNUAL MEETING. Edited by Alfred Blalock, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co. 944.

TEXTBOOK OF SURGICAL TREATMENT INCLUDING OPERATIVE SURGERY. Edited by C. F. W. Blumgart, M.D.

Ch.M. F.R.C.S.F. 2d ed. Baltimore: The Williams & Wilkins Co., 944.

ARTHRITIS AND ALLIED CONDITIONS. By Bernard L. Comroe, A.B. M.D. F.A.C.P. Philadelphia: Lea & Febiger, 944.

INTERNAL MEDICINE. By M. G. Serrys, Ph.D. Springfield, Ill., and Baltimore, Md. Charles C. Thomas, 945.

ESSENTIALS OF ORAL SURGERY. By Wilbur Paul Blair, A.M., M.D. F.A.C.S. and Robert Henry Ivy, M.D. D.D.S. F.A.C.S. 4th ed. with the collaboration of James Barrett Brown, M.D. F.A.C.S. 3d ed. St. Louis: The C. V. Mosby Co. 944.

THE PRECENTRAL MOTOR CORTICES. Edited by Paul Bogy, Urbana, Ill. The University of Illinois Press, 1944.

CONTROL OF PAIN IN CHILDREN. By Clifford B. Ladd, M.D. F.A.C.S., and Robert H. Moon, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co. 944.

COMBINED TEXTBOOK OF OBSTETRICS AND GYNECOLOGY. Revised by J. M. Munro Kerr, LL.D. M.D. F.R.C.P. & S. F.R.C.O.G. Baltimore: The Williams & Wilkins Co. 944.

MANAGEMENT OF REMEDIAL EXERCISES IN MEDICAL AND SURGICAL CONDITIONS. By Noel M. Tidy, 6th ed. Baltimore: The Williams & Wilkins Co. 944.

PRACTICE AND APPLICATIONS FOR STUDENTS, HOSPITAL RESIDENTS, AND PRACTITIONERS. By J. Ross Mackenzie, M.D. D.A. (R.C.P.) & S. Eng. Baltimore: The Williams & Wilkins Co. 944.

AMERICAN MEDICAL PRACTICE IN THE PERSPECTIVES OF CENTURY. By Bernhard J. Stern, Ph.D. New York: The Commonwealth Fund, 945.

MEDICAL USES OF SOAP. Edited by Morris Fishbein, M.D. Philadelphia: London: Montreal: J. B. Lippincott Co. 945.

ENDOCRINOLOGY OF WOMAN. By E. C. Hamblein, R.S., M.D. F.A.C.S. Springfield, Ill. Charles C. Thomas, 945.

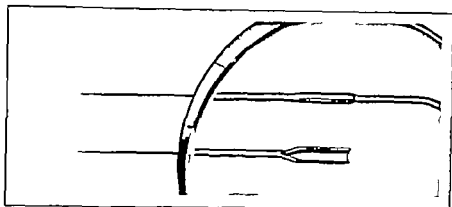
THE RETICULO-ENDOTHELIAL SYSTEM IN SELF-DEFENSE AND ACTIVITY. By Frank Thomas Mosher, Ph.D. Urbana, Ill. The University of Illinois Press, 944.

CLINICAL AND ROENTGENOLOGICAL STUDIES OF ACUTE OBSTRUCTION OF THE SMALL INTESTINES DUE TO ADHESIONS AND BANDS. By Fredrik Koch. Malmo: Svenska Dagbladet Aktiebolag, 944.

PSYCHOLOGY OF INTERNAL DISEASES. By W. Ham Boyd, M.D. LL.D. M.R.C.P. (Ed.) F.R.C.P. (Lond., Dipl. Psych.) F.R.S.C. 4th ed. Philadelphia: Lea & Febiger, 944.

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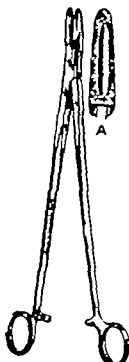
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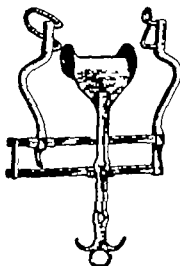
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- TC-200 MASSON needle holder. Chrome plated. 10½ inches. Box lock. Each \$17.50
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GYNECOLOGY AND OBSTETRICS

An International Magazine, Published Monthly

VOLUME 80

MARCH, 1945

NUMBER 3

PANCREATIC COLLECTIONS (PSEUDOCYSTS) FOLLOWING PANCREATITIS AND PANCREATIC NECROSIS

Review and Analysis of Ten Cases

ROLAND D. PINKHAM, M.D., San Francisco, California

IN reviewing the cases of so called pancreatic pseudocyst and suppurations at the San Francisco City and County Hospital some interesting facts were brought out which merit consideration.

The work of Koerte, Lazarus, McWhorter, Opie, Judd, and many others has done much to pave the way for better understanding of the clinical and pathological findings in pseudocysts of the pancreas. Trauma, acute and chronic pancreatitis, and hemorrhagic necrosis have been associated with the development and formation of pancreatic pseudocysts and abscesses. The underlying cause of pancreatitis and hemorrhagic necrosis is still a subject of lively discussion, and it is far beyond the scope of this paper to delve into that phase except to mention some of the related conditions which may be closely associated with the pathogenesis of these cysts.

So called pseudocysts may be formed within the substance of the pancreas as the result of degenerative changes affecting the interstitial tissues of the gland, or adjacent to the pancreas when the corrosive action of the pancreatic ferments has led to the encapsulated accumulations about the gland. The greater

proportion of these cysts is found lying within the lesser peritoneal sac and they usually present according to Koerte in one of three sites: (1) between the stomach and the transverse colon under the gastrosplenic omentum, (2) between the stomach and the liver under the gastrohepatic omentum, (3) between the leaves of the transverse mesocolon. Although these are the usual sites, many bizarre locations may be found. They have been known to dissect retroperitoneally and present in the pelvis.

The wall of the pseudocyst is formed by dense connective tissue of variable thickness. There is no true epithelial lining, but often there is described an endothelial lining which apparently takes its origin from the connective tissue wall. The epithelial lining of the true cyst arises as the result of occlusion of a duct or by epithelial proliferation. It may be destroyed by the necrotizing action of the pancreatic ferment or by pressure necrosis, thus making differentiation between true and false cysts impossible.

Clinical and experimental evidence shows that cysts may be formed secondary to trauma of the pancreas. The history of trauma in cyst formation has been commented upon repeatedly in the literature since the days of Koerte and appears to be associated with

From the Surgical Service of the Stanford University School of Medicine and the San Francisco City and County Hospital.

cystic development in 25 to 35 per cent of the cases depending upon the author and the series quoted. Recent series are inclined to place the figure at 20 per cent or less. Apparently the resulting hemorrhage and trauma in or about the gland is the basis for development of the cyst. The secondary effect of necrosis and enzymatic changes due to liberated pancreatic ferments at the time of injury or subsequently may alter the contents of these cysts in such a degree that they may contain clear straw colored turbid or dark black fluid and in addition may contain particles of sequestered pancreatic tissue. True hematic cysts following trauma usually are nothing more than hematomas of the lesser bursa. They do not show the ravages of chemical alteration by the pancreatic enzymes. Lazarus and Thuroloix and others have produced small cysts by trauma or by injecting necrotizing substances into the pancreas of experimental animals. There is little doubt then that both clinically and experimentally cystic accumulation may arise from traumatic injuries of the pancreas.

The relation of acute and chronic pancreatitis to the production of pancreatic cysts and suppurations is well established. No doubt this makes up a far greater proportion of the cases than formerly recognized. Both true and false cysts may result from pancreatitis. Just how this is brought about is the subject of considerable discussion. Tilger and Dieckhoff suggest that this may be the result of fibrosis throughout the various parts of the gland constricting the ducts with partial obstruction and dilatation distally. This is followed by degeneration of the acinar cells which in turn leads to necrosis of other tissues by the action of the liberated ferments. Though this has never been proved experimentally it seems perfectly logical that it may occur. Retention cysts apparently do occur as a result of partial obstruction of the pancreatic ducts either as a result of fibrosis, calculus or tumor. Opie has shown that ligation of the main pancreatic duct in animals will not lead to the development of cysts but rather to resultant fibrosis and dilatation of the ducts distal to the site of occlusion. The so called *ranula pancreatica* of Virchow. Judd was of the opinion that all

cases of pancreatic cyst are associated with pancreatitis. Although this may not always be the case chronic pancreatitis frequently is found in association with pancreatic cysts. Which is the cause and which the effect is difficult to say though it is reasonable to suppose from the clinical histories as well as from the pathological specimens of reported cases that the inflammatory process most probably precedes the cystic development.

Pseudocysts have been observed following hemorrhagic necrosis of the pancreas by a number of authors, including Francke, Rosenmorsky, Adler, Dressel, Carslaw, McWhorter, Judd and Wangenstein. Although the amount of pancreatic damage in hemorrhagic necrosis often is greater than in traumatic injury the resulting collections would appear to develop quite comparably that is as the result of hemorrhage, necrosis and enzymatic changes. The presence of pathogenic organisms, or biliary and duodenal content which may serve as the activating principle in the resulting hemorrhagic necrosis may bear some relation to the character of the accumulated fluid supuration being far more common in this group.

The frequent occurrence of biliary tract disease in association with pancreatic necrosis and pseudocyst as shown by Archibald, Opie, Judd and others is of great significance. It was Archibald's contention that pancreatitis may be the result of bile entering the pancreatic duct and if this be true that subsequent pancreatic accumulations are the products of necrosis from bile pancreatitis. Judd reported 17 of 41 cases of pancreatic cyst which had associated biliary tract disease. Opie, Whipple, McWhorter, McPhedran and many others have given sufficient clinical proof that biliary tract disease with or without stones, and pancreatic disease can be closely correlated.

It may be difficult to differentiate at times between pancreatic cysts and pancreatic suppurations. Either may develop subsequent to trauma, hemorrhagic necrosis, or pancreatitis. The wall and contents of these cysts may be grossly indistinguishable. It being only a matter of degree of infection which separates the two types. Most writers on the subject believe that infection develops in these cysts sec

ondary to tissue necrosis rather than after primary infection of the pancreas. In those cases of suppurative pancreatitis the inciting organism in all probability is the cause of the pancreatitis as well as the suppuration. Archibald found that when infected bile was injected into the pancreatic duct it led to a more extensive necrotizing lesion of the pancreas than when bile alone was used and suppuration was far more frequent.

Pancreatic abscesses occasionally develop as a result of acute or chronic pancreatitis and usually in association with complete or partial obstruction of the pancreatic duct. The appearance of fat necrosis inflammation interstitial fibrosis and hemorrhage in or about the gland would lead one to believe that the origin of these abscesses is so closely akin to the other pancreatic collections which have been previously described that differentiation may be impossible.

Following the first episode of pancreatitis, the pancreas appears to be more vulnerable to recurrent insults resulting in chronic pancreatitis. As a rule cysts resulting from chronic pancreatitis contain clear or turbid fluid often mucoid in character whereas those resulting from acute pancreatitis or pancreatic necrosis have a tendency to be hemorrhagic in character containing particles of tissue necrosis dispersed within its contents.

Since there seems no infallible way to differentiate at laparotomy or necropsy between hematogenic collections pseudocysts and pancreatic suppurations the diagnosis and classification of these accumulations are subject to wide individual interpretation. It appears logical then in view of what has been said to disregard the term false or pseudo cysts and designate these as pancreatic cysts or collections resulting from trauma (direct or indirect) duct obstruction (calculi tumor inflammation) acute and chronic pancreatitis (infectious chemical) and pancreatic necrosis (infectious chemical vascular). Retention cyst should be used to designate ductal dilatation arising secondary to partial or complete occlusion of the pancreatic ducts whereas true cysts should be limited to denote those of a proliferative hydatid dermoid or congenital origin.

The contents of these accumulations as previously stated may be old blood clear or dark fluid containing particles of necrotic debris. Trypsin when present renders proof that the collection is of pancreatic origin. The amylase content may be low equal to or as often seen markedly elevated as compared to the serum amylase level. If it is low or not above the corresponding blood level its significance is doubtful. But if it is markedly elevated it is significant and indicates that the collection is undoubtedly of pancreatic origin. It is true that in hematoma elsewhere in the body in ascitic fluid and in abscesses and other collections amylase is contained in varying degrees but usually it closely approximates the serum amylase level. Gross discrepancies do not occur in accumulated fluid in the pancreatic region except in collections of pancreatic origin. It is well known that the amylase or lipase determination on proved pancreatic collections can be considerably below the level of the serum amylase. Opie states that they can be totally absent although we have not found this to be the case. Some writers have mentioned the significance of bile in the fluid presuming that if bile is present it must have reached the pancreas by retrograde flow through the pancreatic duct hence lending support to the theory of bile pancreatitis. Altered blood anywhere in the body cavity may give positive bile tests so that the presence of bile in the cystic fluid is of no particular significance. Cultures of fluid from these collections often show growth of *Bacillus coli* and include other pathogenic organisms streptococci staphylococci diphtheroids and so forth. The frequency with which a positive culture is found depends to some extent upon the persistence with which it is sought.

COLLECTIONS SUBSEQUENT TO PANCREATIC NECROSIS

The first 6 cases to be reported are pancreatic accumulations resulting from acute pancreatitis and pancreatic necrosis. The first 4 cases are associated with biliary tract disease. In 1 of the 2 remaining cases no mention was made of the state of the biliary system in the operative report and no gall bladder visualization was attempted. The other case up

posedly had a normal appearing biliary system at laparotomy and no underlying cause could be found for the pancreatic necrosis.

CASE 1. J. S. white American housewife aged 31 years entered the emergency ward of San Francisco Hospital with the story of indigestion intolerance to fatty food, intermittent colic-like pain in the right upper quadrant for the past 14 months. The present illness began on the day before entry with severe abdominal pain which radiated to the back. Her condition on entry was fair. There was tenderness over the entire abdomen with rebound tenderness in the upper quadrant more marked on the left. The patient was found to have pelvic tenderness on rectal examination.

Her temperature was 101.4 degrees F and the white blood cell count was 22,350. Because the patient had a sustained high fever and persistent abdominal pain she was operated upon 5 days after hospitalization with diagnosis of empyema of the gall bladder. Serum amylase on this day was 50 units. The laparotomy showed fat necrosis and bloody fluid in the peritoneal cavity. The gall bladder common duct, and pancreas were not drained. The blood in the abdomen was clotted and the patient returned to the ward in fair condition.

After operation the serum amylase continued to rise and her clinical course grew considerably worse for the next few days. Six days after operation her serum amylase was 1050 units. Two weeks following surgery, gall bladder visualization showed a well functioning gall bladder although many stones were seen. Gradually her fever subsided and she improved steadily although her postoperative course was interrupted with episodes of severe abdominal pain, leukocytosis and marked elevation of serum amylase. Six weeks after entry she was reoperated upon. The gall bladder was removed and the common duct explored. No stones were found in the common duct. A large cystic mass which lay behind the transverse colon was found in the region of the body of the pancreas. This was marsupialized through the transverse mesocolon and the abdominal wall to the left of the umbilicus. The common duct was then drained through a T tube. The postoperative course was moderately stormy. The cystic fluid had a dark brown color and contained necrotic flecks of tissue. It was amylase-positive but contained no organisms on smear or culture. The cyst drained profusely for 6 weeks and then moderately for 4 weeks and finally subsided completely. The serum amylase had returned to normal at this time. Although the cultures were negative for organisms at the time of operation after the tube was inserted into the cystic cavity pancreatic drainage grossly was purulent within a day or so. It contained Bacteroides coli on culture. Pathological sections of the gall bladder showed chronic cholecystitis, cholelithiasis and hyperplasia of the regional nodes. Blood cultures were at all times negative. The patient was

seen in the clinic 6 months after discharge, having no complaints.

CASE 2. J. H. 57 year old male steamfitter entered San Francisco Hospital with the story of having right upper quadrant pain with jaundice intermittently for the past 1 year. Seven or 8 weeks previous to entry into the hospital the pain became quite severe and increased in intensity. Three days before entry he had a sudden onset of knife-like pain in the abdomen radiating to the left shoulder. A second severe attack occurred on the day of entry with severe pain radiating to the right groin from the midabdomen. Abdominal examination showed marked guarding, spasm with rebound tenderness in the left upper quadrant. The temperature was 99.2 degrees F and the white blood cell count was 18,500. Urine contained three plus albumen and a trace of sugar. Serum amylase was 193 units. Leucocytes and x-rays of the Roentgenograms showed a loop of distended small bowel presumably duodenum which may have been slightly enlarged. Gall bladder visualization attempted on two occasions failed to show any duct and no stones were seen. Ten days after entry mass was palpated in the right upper quadrant. The temperature gradually fell and the white blood cell count ranged from 12,000 to 18,000. The patient was operated upon with the diagnosis of a site obstructive cholecystitis. When the peritoneal cavity was opened a large quantity of clear yellowish ascitic fluid was found. A large fluctuant mass was found in the region of the head of the pancreas which appeared reddish-blue in color and had a thick wall. It was aspirated and 2000 cubic centimeters of greenish-brown material was removed which contained flecks of fibrin and necrotic material. The amylase content of this fluid was 475 units. The cyst wall in places was 3 to 4 centimeters in thickness. The cyst was marsupialized through the laparotomy incision. Biopsy of the cyst wall showed chronic inflammatory tissue. The condition of the gall bladder was not noted at the time of operation. Smears and culture of the cystic fluid were reported negative at first but later Staphylococcus albus was reported. The fluid was turbid and contained many polymorphonuclear and plasma cells. After operation the serum amylase ranged from 4 to 7 units on repeated occasions. Excision of skin about the drainage site was slight. Three months after discharge from the hospital he was feeling well and drainage had ceased.

CASE 3. D. G. 45 year old American housewife, with history of intermittent pain in right upper quadrant with jaundice for 3 years. The week before entry she had a sudden onset of severe pain in the right upper quadrant and pain in the pit of her stomach. She felt cold and perspired profusely. When she was brought into the emergency ward of the San Francisco Hospital her temperature was 99.6 degrees F and the white blood cell count was 26,000. Abdominal examination showed a mass 1 centimeter in diameter projecting downward from the midline. There was tenderness over the entire ab-

According to the method of Semmery, normal range is 10 to 50 units.

domen and especially in the left upper quadrant. The impression at that time was empyema of the gall bladder or pancreatic cyst. Gastrointestinal series showed a wide duodenal loop compatible with enlargement of the head of the pancreas. At laparotomy 8 days after entry, fat necrosis was seen and a cystic mass was found in the region of the lesser bursa. The transverse mesocolon was pushed upward by the mass. By blunt dissection the cyst was opened through the transverse mesocolon. When its cavity was entered a large amount of dark purulent material was removed; the exact amount was not noted. This fluid contained a large amount of necrotic tissue, presumably pancreatic in origin. No smears or cultures were taken of the material nor were amylase studies made. The cyst was drained and the wound was closed. The patient ran a rather stormy postoperative course for a day or two but on the third postoperative day the temperature was normal and it remained so. After draining moderately for 6 weeks the cavity closed and the patient was discharged as well. No mention of the gall bladder was made in the operative note.

Ten years later in 1940 she was readmitted with pain in the right upper quadrant, a palpable tender mass and jaundice. Icterus index was 40 upon entry and serum amylase 70 units, blood sugar 202 milligrams per cent. Diagnosis of acute cholecystitis was made and the patient was operated upon. The gall bladder was found distended and filled with many stones. The common duct was explored but no stones were found and no dilatation of the duct was noted. Many adhesions were found in the region of the gall bladder, duodenum and pancreas hanging them to the old incision of the abdominal wall. The pancreas did not appear abnormal at this time. Sections of the removed gall bladder showed chronic cholecystitis and multiple calculi were found in the gall bladder. The patient was discharged from the clinic 6 months later, her diabetes being controlled with small doses of insulin.

Case 4. G.A. 57 year old male mechanic with history of onset of acute abdominal pain 4 1/2 years before entry. The pain originated in the epigastrium traveling toward the left flank. He vomited a small amount of greenish material. The patient stated that he had a similar attack 5 years before. His temperature was 101 degrees F and the white blood cell count of 11,000 had a normal distribution. The abdomen was tender to deep palpation but no masses were felt. The temperature and white blood cell count dropped to normal shortly after entry. The man complained of severe abdominal pain with radiation of pain into the right testicle for the next one or two days. Then the pain gradually subsided and improved. Ten days after entry a mass became palpable in the right upper quadrant. On a subsequent physical showed a very wide but normal palpable mass with enlargement of the head of the pancreas. The gall bladder was not visualized. Blood sugar within normal limits. Three weeks after entry at a rate in a large mass in the pancreatic region.

containing necrotic tissue blood serum and fibrin was drained. Fat necrosis was evident. Cultures of the material showed *Bacillus subtilis*. The patient expired suddenly the following day. Autopsy showed congenital absence of the gall bladder with a stone in the common duct. Between the liver pancreas and the stomach and beneath the transverse mesocolon was a large necrotic mass of tissue and fibrin. A large cystic cavity filled with dark blood was found in the head of the pancreas. A similar but smaller cyst was found in the body of the pancreas. Microscopic sections of the region about the pancreas showed necrosis lymphocytic infiltration with marked fatty degeneration. No normal pancreatic tissue was seen.

CASE 5. A H 58 year old white American carpenter entered San Francisco Hospital a month after onset of severe upper abdominal pain. The initial pain was so severe that he was forced to get off the train on which he was traveling and seek medical relief. The pain and vomiting continued for several days then gradually subsided but he noticed a persistent dull cramping pain in the epigastrum which was aggravated by eating. One month prior to entry into the San Francisco Hospital he had another severe bout of pain which lasted only a few hours. The patient lost a considerable amount of weight during this period of time but denied being jaundiced. Physical examination on entry revealed an emaciated man having a mass in the upper part of his abdomen which measured to be 16 centimeters was smooth globular and gave the impression of being cystic in nature. Percussion was variable from the left to the right in the upper quadrants over the mass. Cystic analysis showed no degrees as the highest total acid serum amylase was 222 units on entry. Glucose tolerance test was within normal limits. Cystic analysis showed no evidence of intracystic gastric lesion. The stomach was encroached upon by a large mass and the duodenal loop was enlarged. Diagnosis of pancreatic cyst was made. At operation a large mass was found behind the transverse mesocolon. This was marsupialized at the site of the abdominal incision. There was evidence of extensive fat necrosis. The gall bladder could not be felt. A week later the cyst was drained by a trocar at the site of marsupialization and 550 cubic centimeters of dark brown fluid was removed. The material which was filled with streaks of necrotic debris had a specific gravity of 1.024 and contained many white and red blood cells. Smears showed gram negative rods and on culture the *Bacillus coli* was found. The fluid contained 550 units of amylase. The blood amylase level remained slightly elevated for several weeks gradually coming down following drainage of the cyst. At the time of the postoperative more than a degree of fever. The white blood cell count was never over 10,000. The patient improved gradually. There was a considerable amount of regression of the mass but the residual cystic mass remained. The cystic fluid was cultured and found to be negative after drainage.

tric pneumograms showed a residual mass in the region of the pancreas which displaced the stomach upward. Gastrointestinal series showed a widened duodenal loop. Cholecystograms showed good concentration of the dye and no stones. A year later a small ventral hernia was repaired which had developed at the site of drainage. At that time gastrointestinal series was reported negative and no calcifications were noted in the region of the pancreas. In repairing the hernia, the peritoneum was opened and the abdomen was explored. Many adhesions were found and a small hard nont cystic mass was felt in the region of the pancreas which was thought to be the vestige of the previously drained pancreatic cyst. The patient is asymptomatic at the present time and no definite mass can be felt on abdominal palpation.

CASE 6 B.W. 34 year old American housewife. Five days before entry the patient had severe abdominal pain and diarrhea. She was taken to a private hospital where morphine sulfate was given to control the pain. Subsequently she was removed to the San Francisco Hospital with the diagnosis of acute cholecystitis. During the 6 months prior to entry the patient had noted that fatty food and starches made her nauseated. Since that time once or twice a week she has had episodes of sharp colic-like right upper quadrant pain which lasted for as long as 1 1/2 hours. Her present attack was similar to the previous attacks but was more severe. On entry she was not in great distress. Abdominal examination showed a mass in the right upper quadrant which was very tender. Her temperature was 99 degrees F the white blood cell count was 8,500 and the icterus index was 5.5. The blood sugar was normal and bile was found in the urine. She was operated upon 6 days after onset of pain with diagnosis of acute cholecystitis. When the abdomen was opened bloody fluid was discovered in the peritoneal cavity fat necrosis was present in the region of the pancreas. There was a cystic mass containing about 60 cubic centimeters of dark brown fluid in the region of the lesser bursa which was drained through a stab wound. The pancreas was hard, swollen and odorated. The gall bladder was of normal size and consistency. The patient drained purulent material after operation but cultures and smears of this material were negative. The patient continued to run a low grade fever and an elevated white blood cell count after operation for several weeks. A month later she was reoperated upon. A mass about 10 centimeters in diameter was found just lateral to the sinus tract which on aspiration yielded 200 to 300 cubic centimeters of pus mixed with necrotic tissue. This abscess apparently was localized at the site of the previously drained pancreatic collection. Drainage of this abscess continued for a month or 6 weeks. The patient made an uneventful recovery. Smears and cultures which were obtained of the cystic fluid at the second operation showed *Streptococcus viridans* *Staphylococcus albus* and gram positive rods, presumably *Bacillus coli*.

COLLECTIONS SUBSEQUENT TO SUPPURATIVE PANCREATITIS

The following 2 cases are illustrative of pancreatic suppurations. The first case most likely resulted from septic hemorrhagic pancreatitis. The second case appears to be one of acute and chronic pancreatitis with partial obstruction of the pancreatic duct with suppuration developing distal to the site of obstruction. Why this does not occur more commonly as we see in obstructions of other glandular structures (kidney liver etc.) is a question. Perhaps it is due to the bacteriostatic action of the pancreatic (proteolytic) enzymes.

CASE 7 H.S. a 30 year old American married housewife entered San Francisco Hospital with the history of abdominal trauma sustained many years before. The patient had been drinking heavily and quit suddenly on the day of entry developed severe abdominal pain. She was brought to the emergency ward of the San Francisco Hospital in mild shock. She was vomiting and appeared acutely ill. Blood pressure was 105/70 temperature 99.6 degrees F. The upper abdomen was markedly guarded to palpation. Roentgenograms were negative for free air in the peritoneal cavity. The white blood cell count was 9,800 and the urine was negative. After operation the patient was sent to the medical ward with a diagnosis of possible alcoholic gastritis. In the medical ward her temperature rose to 102 degrees F and the serum amylase showed 197 units the white blood cell count was 11,000. The Wassermann reaction was negative. Agglutinations for typhoid, paratyphoid A and B and undulant fever were all negative. Gall-bladder studies were not made. Shortly after admission she developed alcoholic hallucinations and was sent to psychopathic ward for 5 days where she continued to have a high fever. Daily determinations of serum amylase during this time varied from 197 to 333 units. Her abdominal findings persisted and she was returned to the medical ward. She appeared acutely ill her temperature was elevated and her white blood cell count fluctuated between 11,000 and 13,000 for the next few days. Gastric pneumograms taken 2 weeks after entry showed a space-occupying lesion behind the stomach and in front of the lumbar vertebrae, "presumably a pancreatic cyst." The patient was taken to surgery and, through midline incision the abdomen was opened. There was no evidence of fat necrosis. A large bulging mass presented itself beneath the transverse mesocolon which was entered through the incision in this structure. The contents of the mass contained frank pus and particles of necrotic tissue. The remaining pancreatic tissue was palpated through the cavity and was found to be stony hard. The cyst was explored and found to be multilocular. On its being converted into a single cavity fragments of

necrotic tissue were removed. The cyst was marsupialized and drained through the incision. The patient made an uneventful recovery. Smears made from the contents showed no bacteria but *Bacillus coli* were cultured. Determinations of the fluid showed it to contain 5,000 units of amylase. The patient developed a secondary collection in the right lower quadrant which, on drainage 10 days later showed thick purulent material containing *Bacillus coli* and which had an amylase reading of 682 units. Serum amylase prior to the drainage of the second abscess was 192 units. The patient was discharged 6 weeks after the second operation with slight drainage from both wounds. The blood sugar was not elevated. She has since recovered completely.

CASE 8. A W 75 year old American housewife for the past 10 years had complained of intermittent episodes of abdominal pain. Her present illness began similarly to previous attacks 3 days prior to entry in San Francisco Hospital. She complained of generalized abdominal pain, nausea but no vomiting. She had had no bowel movements for 2 days. Her temperature was 101 degrees F and the white blood cell count was 20,000. There were no abdominal masses although she was tender throughout the upper abdomen. Urine was negative except for a trace of albumen. Barium enema on entry showed diverticulitis of the colon. A flat plate of the abdomen showed no definite obstruction of the small bowel. The patient was operated upon 5 days after entry with the diagnosis of possible bowel obstruction. Many adhesions were found but no obstruction of the bowel was encountered. Because of her poor condition during the operation a rapid closure was made without a definite diagnosis being made. She died 48 hours later. Autopsy showed acute suppurative and chronic interstitial pancreatitis. Fat necrosis was evident throughout the pancreatic area. She had a small left subphrenic abscess, chronic cholecystitis and cholelithiasis. An islet cell adenoma of the pancreas was an incidental finding. No cultures of the pus were obtained at autopsy.

COLLECTIONS SUBSEQUENT TO CHRONIC PANCREATITIS

The last 2 cases to be reported are presumably pancreatic accumulations following chronic pancreatitis. Both of these patients had long histories of repeated episodes of epigastric and abdominal pain suggestive of chronic pancreatitis. Case 9 apparently resulted from chronic pancreatitis with the cyst lying within the glandular substance distal to the site of partial obstruction of the duct. Case 10 showed pancreatic calcifications associated with chronic pancreatitis. Duct calculi as well as interstitial calcifications were reportedly found at the time of operation. The pan-

creatic collection at the time of surgery was found to lie distal to the site of calcification.

CASE 9. C C 54 year old white American male shipyard worker entered the hospital with a 10 year history of intolerance to fatty food and indigestion. One and one half years ago the patient was seen in the San Francisco Hospital with abdominal pain which subsided soon after entry and he was discharged to the out patient clinic. Five weeks before entry he began having epigastric discomfort, nausea and gradual development of an abdominal tumor. At the time of entry a large mass 8 by 10 centimeters was palpated in the right upper quadrant which extended to the left of the midline. A fluid wave was present. The patient was afebrile and his white blood cell count was 13,000. His serum amylase was 335 units and the fasting blood sugar was 103 milligrams per cent. Cholecystograms showed normal filling and no evidence of stones. Roentgenograms of stomach and duodenum showed a large mass posterior to the stomach pressing downward on the transverse colon. Four days after entry exploration through a left upper quadrant rectus incision revealed a small amount of clear yellow peritoneal fluid and a large dark blue cystic mass under the gastrotocolic ligament. On aspiration of the cysts 4 liters of brownish fluid was obtained. The wall of the cyst was composed of chronic inflammatory tissue. Cultures and smears of the cystic fluid were negative for bacteria. No bile salts were present in the cystic fluid and its amylase content was 85 units. After operation a moderate amount of clear yellowish mucoid material drained from the cyst. No evidence of skin digestion was noted about the sinus opening. The patient was discharged much improved a few weeks later with a draining sinus which became obliterated approximately seven weeks after operation.

CASE 10. G G 39 year old white American sales man entered San Francisco Hospital with the complaint of abdominal pain and vomiting for one week. The patient gave a history of frequent attacks of epigastric pain for many years. He was moderately sick with temperature of 100.6 degrees F and a white blood cell count of 17,000. Abdominal examination showed moderate distention with marked epigastric tenderness. Rectal tenderness was also present. Roentgenograms showed no free air in the peritoneal cavity. The urine was negative and the serum amylase was 417 units. On the following day it was 820 units. The clinical course improved after entry into the hospital despite the rise in serum amylase. The patient was discharged to the out patient department but failed to return. Two and a half months later a similar episode of abdominal pain with vomiting led to his re-entry into the hospital. Abdominal examination showed generalized pain and tenderness and a mass approximately 8 by 12 centimeters could be discerned in the left upper quadrant. Serum amylase on entry was 327 unit. Urine was negative. The blood contained 14,500 white cells. Roentgenogram of the abdomen b 1

acute bowel obstruction but later at post mortem examination suppurative pancreatitis was found. The 3 remaining cases were suspected of being pancreatic cyst preoperatively a suspicion which was substantiated at laparotomy.

A sudden enlargement of the cyst with appearance of shock and intense pain may be produced by massive hemorrhage into the cyst or sudden diminution in the size of the cyst with associated diarrhea shock, and a rigid abdomen may be the result of rupture of the cystic contents into the bowel or free peritoneal cavity. Excess fat is often found in the stool in cases of pancreatic cysts but foamy stools are a rarity.

Little can be added to the long list of diagnostic procedures that have been described repeatedly in the literature. A fact worthy of mention however not previously stressed in the literature is the frequency with which hemorrhagic necrosis and pancreatitis precede the onset of pancreatic collections. No doubt many small collections and hematomas which escape clinical detection are spontaneously absorbed. By careful examination undoubtedly many more of these could be diagnosed.

Roentgenographic examination is a valuable adjunct to our diagnostic procedures. A flat plate of the abdomen may show a silhouette of the cyst. Barium meal may denote the displacement of the stomach by the mass, and the duodenal loop may be widened because of enlargement of the head of the pancreas. Barium enema may show the colon displaced in various directions or encroached upon by the pancreatic tumor. Outlines of the cyst wall by lipiodol injections into the sinus tract following drainage occasionally have been resorted to in cases of retention cysts with duct obstruction. Recently gastric pneumograms have been taken in several of our suspected cases of pancreatic cysts with notable success. Using a modification of the method of Engel and Lysholm our radiologists at the San Francisco Hospital on several occasions have demonstrated retrogastric enlargements of pancreatic origin that could not have been identified otherwise. The posterior gastric wall of the air-distended stomach was thereby used to delineate the pancreas and the retro-

gastric tissue. It has been shown with marked regularity that when the thickness of the retrogastric tissue was greater than the width of the vertebral body the pancreas or the retrogastric tissue was abnormally enlarged. Despite all these diagnostic procedures, often the diagnosis cannot be made preoperatively with certainty.

SUMMARY

Ten cases of pancreatic collections have been presented.

An attempt has been made to classify pancreatic collections on an anatomical as well as on a pathological basis. Since no valid differentiation can be made between "hematic cysts," "pseudo cysts" and necrotic suppurations they should be referred to simply as collections secondary to pancreatic trauma, inflammation or necrosis.

The term retention cyst should be used to designate cystic dilations arising secondarily to partial or complete occlusion of the pancreatic ducts. True cysts should be limited to denote those of proliferative (neoplastic) hydatid, or congenital origin.

Numerous amylase determinations were made of the serum as well as of the cystic fluid in 6 cases. As will be seen, there appears to be no quantitative relationship between the serum and the cystic fluid amylase, either before or subsequent to drainage of the accumulation.

Persistent elevation of the serum amylase following the signs or symptoms of pancreatitis or pancreatic necrosis is significant, indicating the probable development of a pancreatic collection.

The differential diagnosis of pancreatic accumulations from biliary tract disease, perforated ulcer and neighboring pathology may be difficult.

Gastric pneumograms were found to be of material aid in the diagnosis of retrogastric and pancreatic enlargements.

Satisfactory results were attained in all of our cases by single drainage or marsupialization of the pancreatic collection.

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STRENGTH FREQUENCY CURVES IN ELECTRODIAGNOSIS OF EXPERIMENTALLY PRODUCED PERIPHERAL NERVE LESIONS IN THE CAT

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PHYSIOLOGISTS have been interested in the stimulation of nerves and muscles with alternating currents of variable frequencies since Nernst pointed out, on the basis of his polarization theory that the ratio between the square of the intensity and the frequency was a constant.

On the other hand the results of stimulation of nerve and muscle by alternating current have not been employed as indications of the state of the nerve muscle complex in disease or injury to the peripheral nervous system.

There are two observations which have been made by physiologists which are related to the use of the alternating current as an electrodiagnostic procedure. They are (1) the so called optimum frequency or pararesonance and (2) the discontinuity of the strength frequency curve when large fluid electrodes are employed.

As the technique for generating sine waves improved the use of lower and lower frequencies was made possible and this permitted Lullies, Achelis and Renqvist and Koch to point out that the strength frequency curve shows a point at which at a certain frequency

a minimum current is necessary for stimulus. This optimum frequency was said to be situated around 100 cycles per second. This is said to be analogous to the resonance point found in the tuning of electromagnetic oscillations. In order to avoid any confusion with the definition as used in electronics Monnier proposed for this optimum frequency the term pararesonance. Since the components of the electrical circuits in biological tissues are not fully known we elect to use the term optimum frequency.

Although when in the case of the frog's nerve the threshold voltage is plotted against the logarithm of the frequency the curve is said to be U shaped and the two branches are symmetrical about a vertical axis passing through the optimum frequency it will be seen that using larger electrodes and percutaneous stimulation in the case of the cat a different type of curve was obtained.

It was to be expected that the discontinuity found in the strength duration curves when large fluid electrodes were used (Lucas, Davis, Watts and Rushton) and which represent the separate stimulus characteristics of nerve muscle and myoneural junction would be found in strength frequency curves. Coppée pointed out that in the case of a toad's sartorius muscle stimulated under Ringer fluid with large electrodes the strength frequency

From the Department of Nervous and Mental Diseases, Northwestern University Medical School. The work described in this paper was done under contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Northwestern University.

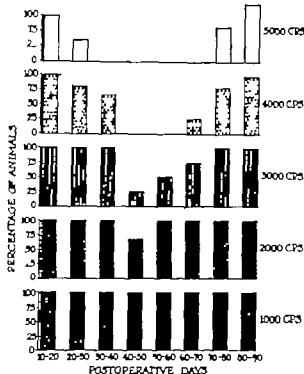


Fig. 3. Five histograms showing the percentage of animals in which contraction could be observed when using 30 milliamperes (root mean square) as the maximal value of current on various postoperative days. In each histogram the parameter is the frequency of the stimulating current.

second. Between 80 and 90 days all contractions at 5000 cycles per second (Fig. 3).

Thus as degeneration progresses, stimulation by relatively large currents fails to produce contraction at higher frequencies and as regeneration occurs and progresses, such currents again become effective at higher frequencies. However the threshold amperage for frequencies of 100 cycles per second and more continuously diminish, but remain high as compared to the normal even after good motor recovery is present. For frequencies of 60 cycles per second and less and particularly for very slow frequencies, one cycle or less per second the threshold amperage increases as has been described by us in the case of the progressive current (9).

When regeneration of a severed nerve is prevented and prolonged denervation produced the threshold amperage for higher frequencies remains high whereas for frequencies of 60 cycles per second and particularly very slow frequencies of one or less cycles per second the

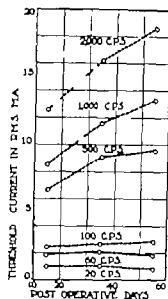


Fig. 4. Threshold current versus elapsed postoperative days in anesthetized denervated cats. The parameter is the frequency of the stimulating current. Each point is an average of data from 3 animals.

amperage diminishes still more than is seen after primary suture and is at its minimum at about the 55th day (Fig. 4).

We have already pointed out that for the normal cat muscle with the percutaneous stimuli with larger electrodes there is no optimum frequency and no symmetry in the two branches of the curve but rather a wide band of from 100 cycles per second to 20 cycles per second, wherein there was a very small change in amperage. At sometime between 20 cycles per second and one cycle per second the amperage rises slightly but at one cycle in 1.33 seconds the amperage is but 1.1 milliamperes (Fig. 5).

As the muscle degenerates and before complete denervation is present this long band disappears and there is a continuous drop of threshold amperage from say several hundred cycles per second to 20 cycles per second. It continues to decrease steadily and gradually to 0.75 cycle per second. It remains the same at 0.5 cycle per second then very slowly and slightly rises if any optimum frequency or band can be determined it is at 0.75 cycle per second (Fig. 6). This is not unexpected since the portion of the curve representing low frequencies is probably related to

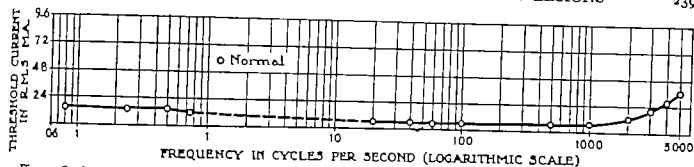


Fig. 5. Optimum frequency band in the strength frequency curve of the gastrocnemius muscle in the normal cat.

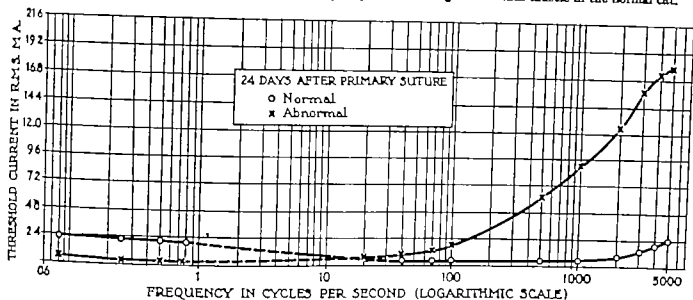


Fig. 6. Optimum frequency band in the strength frequency curve of the gastrocnemius muscle in the cat 24 days after primary suture of the sciatic nerve

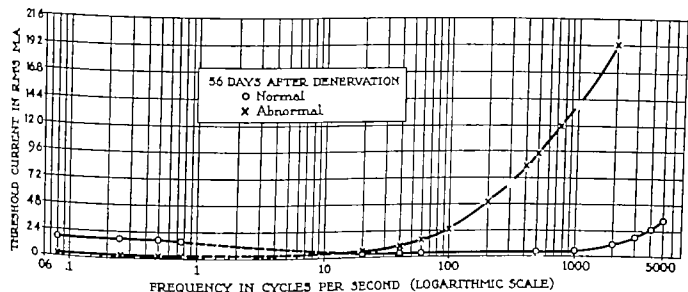


Fig. 7. Optimum frequency band in the strength frequency curve of the gastrocnemius muscle in the cat 56 days after removal of a segment of the sciatic nerve

the alpha curve with longer chronaxie and lower optimum frequency

When the muscle is completely denervated, then the shift of the band of optimum fre

quencies can more readily be seen. There is a continuous diminution in the threshold amperage from say 2000 cycles per second to 20 cycles per second. Then from 20 cycles per

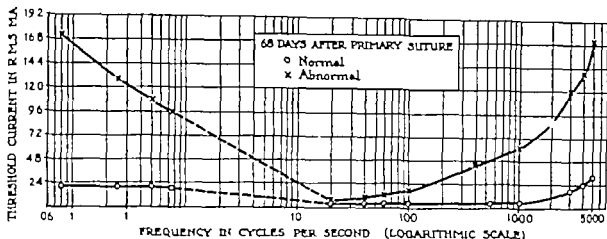


Fig. 8. Optimum frequency band strength frequency curve of the gastrocnemius muscle in the cat 68 days after primary suture of the sciatic nerve

second to 0.75 cycle per second we have no data as indicated by the connecting lines in the illustration. From 0.75 cycle per second to 0.03 cycle per second the threshold amperage remains the same. This corresponds to Coppee's observation of the alpha curve when strength frequency curves were obtained by using large fluid electrodes (Fig. 7).

When the nerve muscle complex shows recovery an entirely different situation is present. As in the other cases, there is a diminution of threshold amperage from 5000 cycles per second to 20 cycles per second; between 20 cycles per second and 0.75 cycle per second we have no data, but at these frequencies the amperage is quite high and steeply increases as frequency diminishes. In this case the optimum frequency would be between 20

cycles per second and 0.75 cycle per second. Although asymmetrical there are two high branches of a skewed curve (Fig. 8).

As has been seen the strength frequency curve in the case of the normal muscle is a continuous one. During the state of degeneration from the earliest date after section at which we have examined animals, 13 or 14 days discontinuity in the curve can be demonstrated. Early in degeneration several usually three discontinuous curves may be seen. One is usually found from 20 to 100 cycles per second; another from 100 cycles per second to frequencies varying from 700 to 3000 cycles per second; and a third from 700 to 3000 cycles per second and upward (Fig. 9).

Immediately before the state of denervation there is a tendency for the curve to show

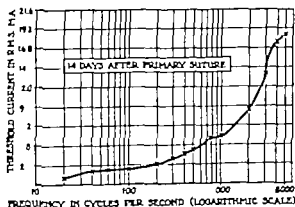


Fig. 9. Strength frequency curve of the gastrocnemius muscle in the cat showing three discontinuities, 4 days after primary suture of the sciatic nerve

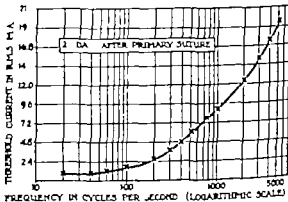


Fig. 10. Strength frequency curve of the gastrocnemius muscle in the cat showing two discontinuities, 34 days after primary suture of the sciatic nerve

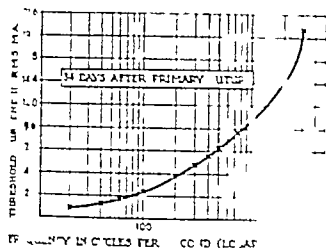
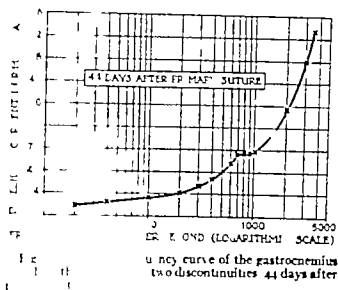


Fig. 11. Strength frequency curve of the cat showing no discontinuities 44 days after primary suture of the sciatic nerve.



but two discontinuities the one at 100 cycles per second to slower frequencies (Fig. 10). During denervation the curve appearing (Fig. 10) During denervation the curve appearing at varying days from 25 to 100 the curve is continuous (Fig. 11).

As recovery begins at varying days from 34 to 50 a discontinuity occurs at frequency from 100 to 1000 cycles per second (Fig. 12). As recovery continues the acute angle between the two curves diminishes until discontinuity disappears. However at this time for frequencies below 100 cycles per second a discontinuity again appears and lasts for a long time after motor recovery (Fig. 13).

DISCUSSION

The characteristic changes from the normal strength frequency curve to that during denervation are

1. An increase of threshold amperage at all frequencies from 20 cycles per second and more relatively less in the case of frequencies from 20 cycles per second to 100 cycles per second and much more for those above 100 cycles per second.

2. With large constant amperage say 20 milliamperes there is a falling out of response of effective stimulation at higher frequencies at first 5000 then 4000 then 3000 perhaps 2000 cycles per second.

3. The long band of optimum frequencies from 20 cycles per second to 100 or at times more disappears and there is a continuous drop of threshold amperage to 20 cycles per

second and a steady but gradual decrease to 10 cycles per second.

4. The appearance of discontinuities in the strength frequency curve in number most constant from 100 to 1000 cycles per second and then from 1000 cycles per second to 700 to 800 cycles per second and a third from 700 to 1000 cycles per second and upward.

The changes during denervation are

1. The threshold amperage for higher frequencies remain high whereas for frequencies of 60 cycles per second and particularly very slow frequencies of one or less cycles per second the amperage diminishes still more than is seen after primary suture and is at its minimum at about the 55th day.

There is a shift of the band of optimum frequencies so that there is a continuous drop in amperage from 2000 cycles per second to 20

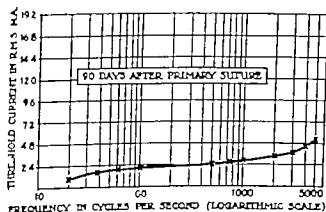


Fig. 13. Strength frequency curve of the gastrocnemius muscle in the cat showing two discontinuities, 90 days after primary suture.

cycles per second, then from 20 cycles per second to 0.75 cycle per second no data are available however from 0.75 cycle per second to 0.08 cycle per second the threshold amperage remains the same indicating a band of optimum frequencies extending as low as 0.08 cycle per second.

3 The strength frequency curve is continuous.

During regeneration there is a diminution of threshold amperage from 5000 cycles per second to 20 cycles per second. Between 20 cycles per second and 0.75 cycle per second we have no data, but at 0.75 cycle per second the amperage is quite high and increases steeply as frequency still further is diminished. In this case although asymmetrical there are two high branches of a skewed curve. A discontinuity reappears at frequencies of from 700 to 1000 cycles per second. The acuteness of the angle between the two curves then progressively diminishes and a continuous curve at frequencies of above 100 cycles per second results. At the same time a discontinuity at frequencies below 100 cycles per second appears and continues long after motor recovery has occurred.

CONCLUSIONS

1 The threshold amperage at various frequencies in the normal degenerating de-

nervated and recovering state of muscles is described.

2 A shifting of the band of optimum frequency to low frequencies below one cycle per second is characteristic for degenerating and denervated muscle.

3 The appearance of two equally high branches of a skewed curve is characteristic of recovering muscle.

4 During early degeneration at least three discontinuous curves may be recognized later but two. During denervation the strength frequency curve is continuous. During regeneration it again becomes discontinuous.

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THE FASCIA-PATCH TRANSPLANT IN THE REPAIR OF HERNIA

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ALTHOUGH the surgical techniques devised by Bassini in 1889 and Halsted in 1890 contributed a marked advancement to the prevalent ideas of radical cure for inguinal hernias it is a recognizable fact that the incidence of recurrence following operation is still too high this is evidenced by the development of the many modifications of the original operations of these men to the present date. Reports from various hospitals and large clinics indicate that the rate of recurrence of all hernias varies from 1 to 10 per cent for the indirect type and from 10 to 25 per cent for the direct type. These figures alone indicate that the problem of inguinal hernia repair is as yet not completely solved.

However in surgical circles there still seems to be a universal agreement that the repair of a defective abdominal wall which Bassini and Halsted considered an essential part of their operations is a fundamental factor in the successful repair of inguinal hernia. Consequently in those more difficult cases in which the defect in the abdominal wall cannot be obliterated by the approximation of the internal oblique muscle and the conjoint tendon to Poupart's ligament without undue strain on the retaining sutures other methods were devised. Among the better known techniques in such cases are the relaxing incision in the lower rectus sheath to reduce the tension on the sutures uniting Poupart's ligament to the internal oblique muscle and conjoint tendon and the use of transplanted fascia by which the abdominal wall defect is obliterated. Transplanted fascia has been used for this purpose both as fresh autogenous and as preserved animal grafts it has also been employed both in the form of a patch and in strips of interlacing sutures.

Although McArthur in 1901 was probably the first to use fascia in the form of sutures in the repair of inguinal hernia, it was Kirschner in 1909 who made the first systematic study on the transplantation of free fascial grafts he reported many successful free fascial transplants for various purposes and placed the method on a sound working basis. Although he did not establish the viability of transplanted fascia by his experiments very little has been added to the practical value of his method. In the same year 1917 that Lewis published experimental and clinical evidence showing the rehabilitation of transplanted fascia Nageotte attracted considerable attention by reporting his results in the transplantation of dead grafts. He successfully repaired anatomic defects in tendons of living animals by replacing the defect with pieces of tendon which had been preserved in alcohol. Experimental work by Gallie and Le Mesurier in 1924 showed that the transplanted fascia became surrounded by a delicate vascular membrane which vascularized the fascial fibers of the graft. The popularity of the use of fascia in the form of sutures in hernia repair is probably due in a large measure to the enthusiastic reports of these men. Being stimulated by the reports of Nageotte and Gallie and Le Mesurier Koonz later reported favorably upon the use of preserved ox fascia used both as a patch and in strips as sutures. However Horsley's work in 1931 led him to the conclusion that preserved fascia is inferior to fresh autogenous fascia when transplanted.

When the treatment of hernia by means of transplantation of fascia lata patches first came into prominence it was believed for a time that the difficulties of a radical cure for hernia had been overcome but with the revival of the use of fascia transplants in the form of strips as suture material by Gallie and Le Mesurier in 1921 the popularity of the



Fig. 1. A larger direct inguinal hernia successfully treated by the fascia patch method. This hernia was of several years' duration with progressive increase in size. Middle-aged negro. At time of operation, large nonhealing ulcer was present on lower posterior aspect of scrotum. No previous hernia repairs had been attempted.



Fig. 2. Large indirect inguinal hernia of 6 years' duration in a 65 year old white male successfully repaired by fascia patch method. Previous Bassini type of repair had failed. Ulceration on the left lower aspect of the scrotum showed malignant changes and the area was excised at time of operation.

fascia patch method diminished. However members of the surgical staff of the John Sealy Hospital have used this method over a period of years and a review of the results leads us to the belief that the procedure should have a definite place in the surgeon's armamentarium.

In a 28 year period beginning in 1916 and ending in 1944, we have used the fascial patch transplant method in 175 patients who presented themselves for cure of hernia. A breakdown of this group showed that of the 175 cases operated upon 93 patients had the direct type of hernia on which 65 previous hernia repairs had been attempted but failed. Forty patients with the indirect type of hernia reported 12 previous operations with recurrence and 42 patients with various forms of ventral and incisional types of hernia reported 30 previous surgical procedures terminating in failure. As was expected this analysis indi-

cates that the ventral and direct types of hernia offer the greater problem in obtaining a permanent cure (Figs. 1 and 2). The fascial patch method was used only in severe cases in which it was obvious that the usual types of hernia repair would terminate in failure. This is evident by the fact that these 175 patients had had 108 previous operations which had failed. We have not used the patch in ventral hernia when it has been possible to bring the muscle and fascia margin of the hernial ring together. Some of these have been very large and the most severe tests of all hernias are in the postoperative ventral type with any procedure.

Since our patients reside over the entire State of Texas we have been able to obtain reliable periodical, postoperative examinations in only 129 of these 175 patients. This group of 129 patients with hernias had had 80 previous repairs which failed. Postoperative

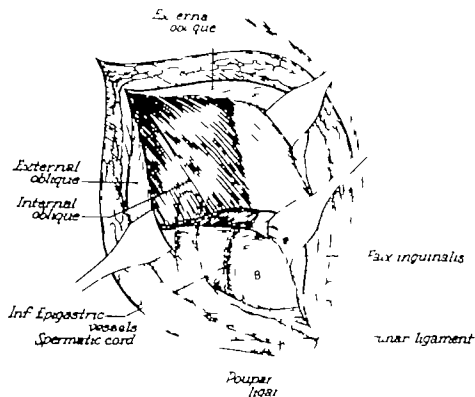


Fig 3. A diagrammatic illustration of the repair indicating the various structures which the fascia patch accurately identified before the successful implantation of the fascia patch. The repair can be anticipated. A Area of origin of the hernia and the fascia patch leaves the abdominal cavity through the internal oblique muscle and the inguinal canal with the spermatic cord. B Area of the fascia patch which is sutured into the abdominal wall. The hernia protrudes and passes through the abdominal wall into the external abdominal ring.

follow ups of this group of patients who were treated by the fascia patch transplant method revealed failure and recurrence of the hernia in 14 cases. We believe that the unfollowed cases would show few recurrences since these patients would probably have returned for treatment had further trouble resulted (Table I). An analysis of this group of 129 cases reveals that the greatest incidence of failure by the use of the fascial patch transplant is in the ventral type of hernia and the lowest incidence is in the indirect type. In 30 cases of indirect hernia reporting 10 previous operations which failed there was 1 recurrence while 33 patients with 29 previous operations for ventral hernia had 6 failures by the fascial patch transplant method. Also 7 failures of the method were found in 66 patients with direct hernias who reported 41 previous operations.

In the 14 cases in which the method failed the recurrence was apparent within 6 months

in the majority of cases and with one exception which was discovered after 18 months all failures were apparent within 1 year after operation. All the other cases reported as

TABLE I.—HERNIA REPAIR BY FASCIA PATCH TRANSPLANT

129 Operated Cases 1916-1944 with Follow-ups

Type	No. of cases	Previous operations with recurrence		Fascia patch method with recurrence	
		No.	Per cent	No.	Per cent
Indirect hernia	30		33.33		3.3
Direct hernia	66			7	10.6
Ventral and incisional hernia	33	29	87.87	6	18.18
Total	129	60	46.5	13	10.1

Table I. An analysis of the series of 129 hernia cases treated by the fascia patch method according to the type of hernia indicating the number and percentage of failures by the fascia patch method as well as that fail therapeutically on other types of repair which failed before the fascia patch method was used in each group.

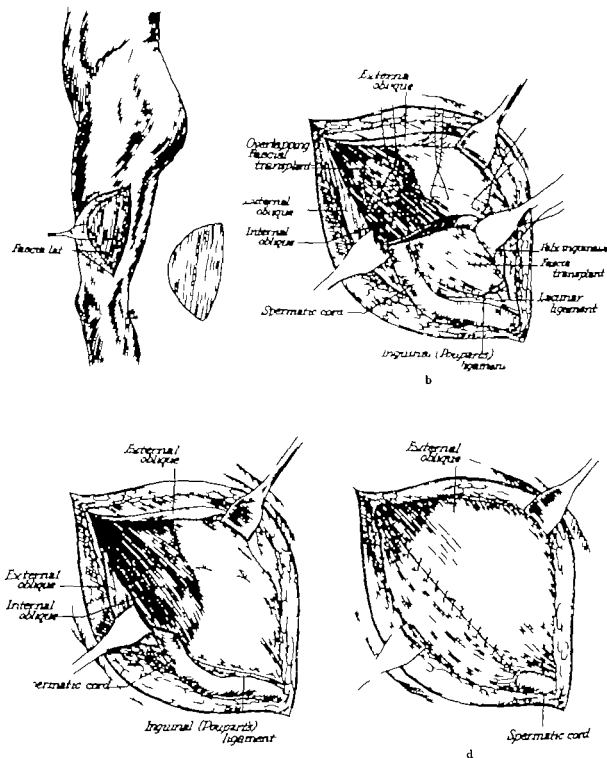


Fig. 4. a, Fascia patch excised from the thigh and notched for repair of inguinal hernia. b, Fascia transplant in place, firmly sutured to the lacunar and Poupart's ligaments before its upper edge is anchored high up under the conjoined tendon, and internal oblique and transversus

muscles. c, Edge of internal oblique muscle and conjoined tendon buttressed to Poupart's ligament over the fascial patch but below spermatic cord. d, External oblique aponeurosis sutured to Poupart's ligament over spermatic cord down to superior crus of external abdominal ring.

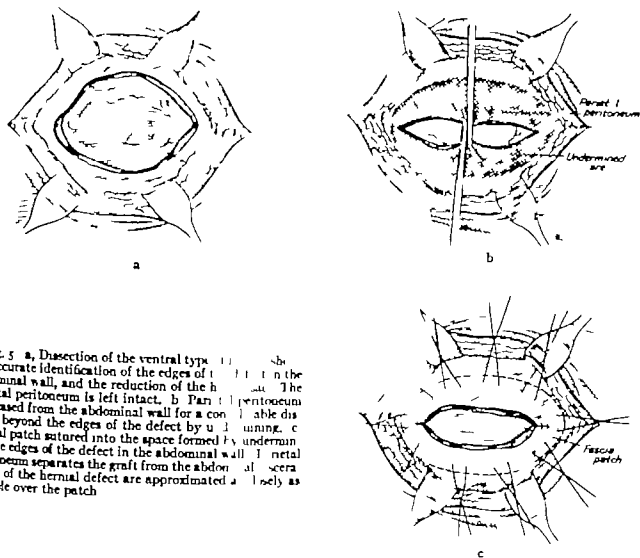


Fig. 5. a, Dissection of the ventral type hernia showing accurate identification of the edges of the defect in the abdominal wall, and the reduction of the hernia. The parietal peritoneum is left intact. b, Parietal peritoneum is released from the abdominal wall for a considerable distance beyond the edges of the defect by undermining. c, Fascial patch sutured into the space formed by undermining the edges of the defect in the abdominal wall. The parietal peritoneum separates the graft from the abdominal viscera. Edges of the hernial defect are approximated as closely as possible over the patch.

failures of the method were anticipated due to such complications as severe wound infections and the development of a sudden gastric hemorrhage followed by anemia and ascites during convalescence. In 2 other failures difficulty was encountered during the operation in obtaining firm tissues on to which to suture the fascial patch transplant; the patients becoming extremely obese and having flabby musculature.

The analysis of this series of cases leads us to believe that the use of the fascial patch transplant in the radical cure of hernia is a procedure that deserves more merit than is usually accorded this method. This is especially true when it is borne in mind that all cases in this series were severe in nature and that the operative procedure was carried out by 13 different surgeons, the majority of whom

were still in the process of acquiring their graduate surgical training. We are impressed by the results obtained by the fascial suture method as advocated by Gallie and Le Mesurier but the proper use of the fascial patch transplant is an anatomical procedure in that it is a replacement of deficient tissue in the defect of the abdominal wall. In comparison with the fascial suture method the operation is relatively easier, is of shorter duration, requires less handling of tissues and causes no distortion of surrounding tissues. If the principles of technique and wound healing are borne in mind when the operation is performed the fascial patch transplant method should enjoy greater success than has been universally accorded it in the past.

The technique of the patch method of fascial grafts for inguinal hernia repair as used



Fig. 6

Fig. 7

Fig. 8

Fig. 6. An indirect inguinal hernia of long standing in middle aged white male successfully repaired by fascia patch transplant. Abdominal rings and inguinal canal were markedly dilated.

Fig. 7. Same patient shown Fig. 6, one month after

operation. No bulge on lateral surface of left thigh here (fascia) as removed for hernia repair.

Fig. 8. Same case as shown in Figs. 6 and 7 showing herniation of muscles of the thigh in area here (fascia lata) as excised one month previously.

by us is not complicated but is relatively simple. We have used it as described here since 1916 and have found no alterations in the procedure necessary since that time. The type of anesthetic used makes very little difference if any as regards the success of the operation itself provided the vomiting, retching, coughing and straining which frequently follow the use of a general anesthetic can be eliminated or kept at a minimum. For this reason in a great majority of the cases reported in this series the operation was carried out under local anesthesia. The skin is infiltrated with 0.25 per cent novocain with epinephrine just along the line of incision above Poupart's ligament. The skin and Scarpa's fascia are incised and bleeding points are clamped. About 20 cubic centimeters of the novocain solution is then injected just beneath the aponeurosis of the external oblique muscle above the area of the internal abdominal ring. This infiltration completely blocks the ilio-inguinal and iliohypogastric nerves before they are exposed. During the few minutes it takes for this injection to complete the anesthesia, the bleeding points of the subcutaneous tissue are

ligated. The aponeurosis of the external oblique muscle is then split in the direction of its fibers in such a manner that the line separation of these fibers passes through the height of the superior crus of the external abdominal ring. By retracting the opposing edges of the split aponeurosis the spermatic cord and hernial sac are exposed. The hernial sac is opened, separated from the spermatic cord structures and the ilio-inguinal and iliohypogastric nerves and is cut across after being ligated at the internal abdominal ring. The conjoint tendon, the internal oblique muscle, transversalis fascia, and Poupart's ligament are exposed as in the usual hernia operation. It is at this point one must decide whether or not it will be necessary to use a fascial transplant. If it is to be used a piece of fascia lata is excised from the lower or middle one-third of the lateral side of the thigh (Fig. 4 a). Here the fascia lata has no posterior attachments to the underlying muscles and is more easily obtained than in the upper thigh. The size and shape of the 'patch' excised from the fascia lata must vary with the dimensions and configuration of the defect to

be repaired. It must be borne in mind that the patch must be larger than the defect to allow overlapping of its edges for the strength of the repair depends both on the type and the amount of union by fibrosis between the graft and the overlapping edges of the defect. A notch is cut in one end of the fascial transplant to receive and fit snugly around the spermatic cord where it leaves the abdomen. Before the graft is put to place one must make sure that all loose areolar and fatty tissues have been removed from the graft and the structures to which it is to be sutured to insure a firm union between the graft and the edges of the defect (Figs. 4 a b c and d). The graft is transferred to the inguinal wound with its upper edge placed beneath the muscle and stitched with mattress sutures to the under surface of the internal abdominal oblique and transversus muscles. The lower edge is secured to the shelving portion of Poupart's ligament either by several mattress sutures or by a continuous suture obtaining as much surface contact between these two structures as possible. The spermatic cord is brought out through the notch in the graft at the point where it leaves the abdomen. The mattress sutures through the internal oblique muscle and conjoined tendon are not tied until the inferior edge of the graft has been firmly attached to Poupart's and the lacunar ligaments. The internal oblique muscle edge and conjoined tendon are then buttressed to Poupart's ligament, as in the Bassini operation and the external oblique is sutured to Poupart's ligament in the same way. The repair of the direct or indirect hernia by this method is practically the same since the areas reinforced by the fascia patch graft covers both Hesselbach's triangle and the edges of the internal abdominal ring. It is especially important in repairing the direct hernia that the corner of the fascia patch be securely sutured and anchored not only to the shelving portion of Poupart's ligament but also to the lacunar ligament. In the indirect hernia special attention is called to the fact that the notch cut in the fascia patch to receive the spermatic cord should be sutured snugly around the cord but not so tightly as to interfere with circulation through the spermatic cord.

The repair of a ventral hernia by the fascial patch method is similar to the technique used in repairing an inguinal hernia. The patch must be cut of such configuration and size as to allow considerable overlap of the surrounding tissues of the defect to insure enough area of contact between the two in order that a union may be obtained strong enough to withstand the physiologic stress and strain. The graft is sutured to place below and beyond the muscular edges of the defect in the abdominal wall by mattress sutures (Figs. 5 a b c). When possible the edges of the defect are imbricated or approximated over the transplant the line of suturing running parallel to the fibers of the surrounding tissues and of the graft. Although the graft is placed below the muscular edges of the defect, the peritoneum or omentum should intervene between the graft and the abdominal viscera to prevent the formation of dangerous adhesions which may terminate in intestinal obstruction.

We have also used the fascia patch in 2 cases of diaphragmatic hernia not included in this series with good results. The intrathoracic approach was used the fascial patch was sutured over the defect to the superior surface of the diaphragm in an overlapping manner. The success of the procedure was verified by subsequent x-ray studies as well as by the remission of symptoms. One of these patients died 2 years after the operation from other causes and at autopsy the diaphragm was found to be in tact the fascial patch being firmly adherent to the bed to which it was sutured. There were also firm adhesions between the superior surface of the graft and the visceral pleura of the lung on one side and between its inferior surface and the gastric serosa on the other.

OBSERVATIONS

The majority of failures previously reported are probably due to errors in technique and possible disregard for certain fundamental principles of wound healing. Gallie and Le Mesurier as well as Koontz and Haas have shown clearly by their investigations that the union between muscle aponeuroses and tendon is by the formation of scar tissue and that there is no proliferation of the essential cells of such tissues. Scar tissue differs from

fascia in that although it is composed of similar white fibers, these fibers are loosely arranged and irregular and when subjected to constant strain show a tendency to stretch. This fact indicates that the firmness of union between the graft and surrounding tissues is directly proportional to area of contact and union between the graft and the structures to which it is sutured (Fig 6). The strength of the union depends on the care with which areolar tissue has been removed and prevented from intervening between the graft and its attachments to muscle or ligaments. Union which is produced by newly formed connective tissue will range from the loose texture of areolar tissue to the firmness of ordinary scar. Actual scraping and scarification of the contacting surfaces of the graft will produce firm scar. Koonitz also obtained a firmer union by cutting away the surface of the muscle to be sutured to the fascia. This was verified by the experimental work of Haas which showed that in the union of muscle to fascia the perimysium, endomysium and the variable cellular elements of the transplanted fascia play the major rôle. In the 6 patients of our series whom we have reoperated upon we have found that there was no absorption of the graft, but that failure was due to either inclusion of areolar tissue in the plane of union between the graft and conjoined tendon with consequent excessive stretching or insufficient area of actual contact between the graft and its bed to obtain a union strong enough to withstand the normal physiological strain. In such cases in which mechanical difficulties prevent placing the graft in actual contact with surrounding tissues over a sufficient distance to obtain enough scar tissue union to withstand the physiological strain the fascial patch method is not indicated and the fascial suture should be used as the strength of the union here depends on the suture itself and the tissues into which it is laced (Fig 7).

Gratz points out that failure of many fascial patch transplants was due to the disregard of the physiological principles of stress and strain. A combination of shearing and tensile stress may result in the disintegration of the transplant unless it is cut parallel to its fibers, and placed in its bed so that its fibers run

parallel to those of Poupart's ligament, or those of the rectus sheath when used in ventral hernias.

The blood supply to the fascial transplant is not an important factor as the viability of the graft is dependent on the seepage of lymph through its spaces. However to insure adequate lymph supply to the graft, it again becomes important to remove adequately all coverings of loose areolar and fatty tissues from the graft before it is sutured into place.

Koonitz and Hertzler advocated the tying of sutures and ligatures tightly when the transplant is being fixed to the surrounding tissue. This not only insures close contact of the graft to its attaching structures, but also produces fibrin formation by traumatizing the muscle and leads to fibrosis upon which depends the union. Tight ligatures will cause no necrosis because of the rich blood supply in muscle.

In many of our cases bulging has occurred at the site from which the transplant was taken from the fascia lata. In most of these cases no unfavorable symptoms occurred except the noticeable herniations of the vastus lateralis muscle (Fig 9). In time these deformities gradually disappear possibly due to the contracture of a layer of scar tissue which forms in that area. Foshee in a recent study concluded that there is a regeneration of the excised fascia lata. In several cases in which we have again operated upon the thigh for purposes of obtaining additional amounts of fascia lata for various reasons, we have found conditions both grossly and microscopically identical to those described by Foshee. Since we have never observed the redevelopment of the strong middle layer of fibers which run in a vertical direction but have only found the reformation of the thinner and weaker outer and inner layers of the fascia lata, we are not inclined to consider this phenomenon as a true regeneration of the fascia lata, but rather the formation of a layer of scar tissue in which the direction of its fibers is influenced to a great extent by the forces of stress and strain from the underlying active muscles of the thigh. Certain members of our group have overcome this difficulty of early bulging of the thigh by obtaining the fascial transplant

from the posterior border of the fascia lata just above the midpoint of the thigh. At this level the underlying vastus lateralis muscle is covered by an aponeurosis from which its muscle fibers arise. Herniation is prevented by the suturing of the cut edge of the fascia lata to the aponeurotic origin of the vastus lateralis. Since no unfavorable symptoms have been produced by the herniation of the thigh muscles through the donor site of the fascia lata patch this procedure may be considered as of minor importance.

In our group of cases various types of suture material have been used namely silk linen cotton and chiefly chromic catgut without any appreciable differences in the end result of the operation.

CONCLUSION

We believe that the use of the patch type of free fascial transplant in the surgical cure of difficult and large hernias is of definite value in selected cases and that proper observance of certain principles of technique

and wound healing in its use will result in a greater degree of success than the method has enjoyed in the past.

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TOTAL PANCREATECTOMY TOTAL GASTRECTOMY TOTAL DUODENECTOMY SPLENECTOMY LEFT ADRENALECTOMY AND OMENECTOMY IN A DIABETIC PATIENT RECOVERY

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THE surgery of pancreatic tumors has become well established as a result of experiences in recent years. It is not only possible to resect large portions of this organ but its total extirpation can now be envisaged. The purpose of this report is to record an instance of very radical attack upon cancer of the body of the pancreas that had extended on to the stomach, into the left adrenal gland, and had metastasized to the omentum and glands of the lesser curvature of the stomach. The patient's history is also of interest because he was diabetic before operation. The diabetes was not due to destruction of pancreas by tumor

F. W. (32858) white male, 53 years of age, was admitted to the medical service of one of us (H. T. R.) February 24, 1944 because of watery foamy stools several to as high as 20 a day for the previous 2 years. There was some abdominal pain at first but this did not continue. There was loss of 50 pounds in weight during this period, yet his appetite remained "ravenous." A complete examination was carried out. The blood was normal. The presence of rather typical steatorrhea was confirmed. He was found to be rather severely diabetic and required 60 to 90 units of insulin daily with carbohydrate intake of 400 to 900 grams and total caloric value of daily diet varying from 2500 to 3500 calories. Roentgenographic examinations of stomach, duodenum, chest and colon were negative. In surgical consultation (A. B.) it was believed that laparotomy was not indicated as he was improving on medical management and was having no pain.

He was discharged from the medical service May 14, 1944. There was no pain, he had gained 37 pounds in weight. Pancreatin seemed to have had no effect upon the number and quality of the stools. The latter at first contained much fat but later this was

reduced by decreased dietary fat; they continued to be soft.

He was readmitted August 24, 1944, because of moderately severe icterus of 3 weeks duration pruritus 1 month abdominal pain in right upper quadrant, at times very severe 1 month. Improvement in diarrhea was noted in that during the first week in the hospital he had only two stools a day. Direct van den Bergh 5.6 milligrams per cent indirect, 7.5 milligrams per cent. Examination of the abdomen was negative except for moderate smooth enlargement of the liver. The gall bladder was not palpable.

Exploratory laparotomy was now thought to be indicated and was performed September 7, 1944, as follows (Fig. 1).

1. The abdomen was entered through a high midline incision. It was immediately apparent that the contracted greater omentum although not adherent to surrounding structures contained numerous spherical metastatic nodes. Before anything further was undertaken the entire redundant portion of omentum was resected by incision along the attachments to transverse colon. The gall bladder appeared normal and contained no stones. It was not distended. The common duct was slightly enlarged.

2. Exploration revealed no gravitational metastases in the pelvis, nor on the peritoneum and there were no metastatic nodules in the liver. The stomach appeared to be bound down by adhesions on its posterior wall. The gastrosplenic omentum was divided and the transverse colon was retracted downward. It now became evident that the primary growth was in the body and tail of the pancreas, that there was direct extension into posterior gastric wall and especially into the nodes along the lesser curvature. The latter formed a dense matted mass almost to the esophagus.

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This study was aided by The Charles and Mary F. S. Worcester Memorial Fund of The University of Chicago.

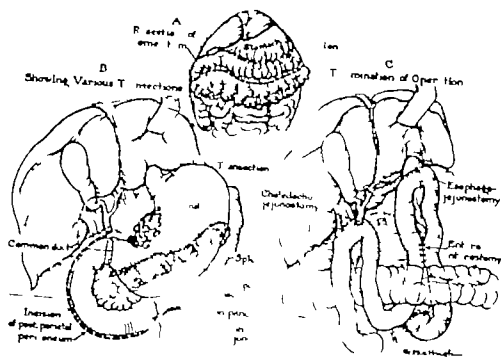


Fig. 1. A. Resection of stomach. B. Various T incisions. C. Transection of jejunum.

The duodenum and head of the pancreas were mobilized by incision of peritoneum along the greater curvature of the duodenum.

The ligament of Treitz was transected and the duodenojejunal junction was mobilized. The superior mesenteric vein was exposed below its emergence from beneath the neck of the pancreas. The duodenojejunal junction was transected with invagination of the distal stump.

4. The right and left gastric vessels were divided and ligated. The head of the pancreas and duodenum were further mobilized and elevated. By sharp dissection the neck of the pancreas was elevated from the superior mesenteric vessels. The duodenum and the head of the pancreas were retracted downward and the common duct was transected at the level of the upper border of the first segment of the duodenum. Below this level it was apparent that the common duct was infiltrated and constricted by neoplastic extension from the pancreas. The duodenum, head of pancreas, and lower stomach were now fully mobilized.

5. The right hand was passed over the diaphragmatic aspect of the spleen and the splenodiaphragmatic ligament was divided. The spleen was brought downward and medially to mobilize the tail of the pancreas and the

greater curvature of the stomach. The spleno-jejunostomy was divided.

6. Dissection to elevate the entire body of pancreas en masse with the stomach was begun at the left of the level of the superior mesenteric vessels since the head of the pancreas and duodenum had been mobilized up to that point. In dissecting free the body of the pancreas the latter fragmented and seemed to be completely replaced in its central portion by tumor which was also densely adherent to posterior upper retroperitoneal tissues. All gross evidence of tumor and pancreas was elevated. The spleen was elevated and this brought up the tail of the pancreas. As the involved mid portion of body of the pancreas was being mobilized it became apparent that the left adrenal gland which was adherent to it because of tumor infiltration was also being mobilized for excision.

7. The entire stomach, entire pancreas, entire duodenum, left adrenal, and spleen were now elevated over the left costal arch. The first long loop of jejunum was brought up through a hiatus in the transverse mesocolon to the posterior aspect of the cardiac end of the stomach and attached to it by interrupted silk sutures. The stomach and other structures were then cut away, the level of transection being about $1\frac{1}{2}$ centimeters below the

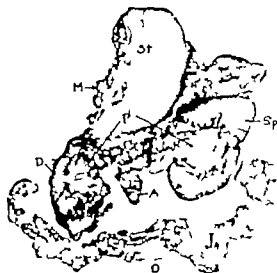


Fig. 2. Surgical specimen consisting of St. practically the entire stomach, D. entire duodenum, P. entire pancreas with C. carcinoma arising in body and tail, A. left adrenal gland, Sp. spleen, O. entire retracted omentum riddled with tumor metastases. M. metastases along lesser curvature of stomach.

esophagogastric junction. Anastomosis between jejunum and esophagus, that had attached a narrow cuff of gastric wall about 1½ centimeters in width was then carried out with two rows of interrupted sutures. An enteroenterostomy was performed between afferent and efferent jejunal loops below level of transverse mesocolon.

8. The second long loop of jejunum was brought upward anterior to transverse colon and choledochojejunostomy was performed, two rows of interrupted silk sutures being used. Interrupted sutures were then placed between the jejunum distal to the latter anastomosis and the falciform ligament to support this anastomosis.

9. The abdomen was closed with Pezzer catheter drain in left upper quadrant and large gauze pack inserted within a sheet of perforated silkoid to serve as a Mikulicz type drain. At the close of the operation there was no macroscopic evidence of carcinoma remaining in the abdomen.

The duration of operation was 5 hours 43 minutes. Infusions of 100 g. operation consisted 2800 cubic centimeters blood, 3000 cubic centimeters saline, 800 cubic centimeters gelatin. Blood pressure at onset of operation was 120/70; at close of operation 110/65. There was no shock at any time.



Fig. 3. Photomicrograph of section from carcinoma of the body of the pancreas $\times 6$.

The surgical specimen illustrated in Figure 2 and the total weight was 856 grams. It consisted of practically the entire stomach, duodenum, pancreas, spleen, omentum and left adrenal gland. The mid-portion of the body of the pancreas and the tail were replaced by carcinoma. The gross appearance of the proximal portion of the body of the pancreas, the neck and head was normal except for an extension of tumor along the superior margin that infiltrated and obstructed the proximal portion of common duct behind the first segment of duodenum. Histologic study revealed a typical duct cell carcinoma of the pancreas (Fig. 3). Slightly of the uninvolved pancreas revealed typical degenerative changes in the islets characteristic of diabetes (G. Gomori).

The postoperative course was remarkably smooth. Nothing was received by mouth for 8 days. Casesin digest and glucose were given intravenously for nutrition. The data concerned with parenteral fluid administration during the first 8 days postoperative are shown in Table I. Food by mouth was then gradually increased until he received a full diet by the end of 13 weeks.

Twelve and one-half months after operation the patient clinically was in fair condition. If was ambulatory. He could have been previously discharged from the hospital but was retained for metabolic studies. The weight was stabilized at 55 to 57 kilograms. The diarrhea persisted despite administration of pancreatin. Examination of the abdomen 4 months after operation revealed metastatic nodules in the abdominal wall beneath the umbilicus and in the left paraumbilical region. There was

TABLE I—INTRAVENOUS FLUIDS BLOOD SUGARS ETC DURING FIRST 8 DAYS AFTER TOTAL PANCREATECTOMY AND TOTAL GASTRECTOMY

Day of operation	5% Amra 5% glucose c.	Gelatin saline	5% Glucose c.	Saline c.	Blood	Plasma c.	Urine Vol	Glucose urine gm	Insulin amounts		Blood sugars mgm %			
									Prot.	Reg.	6 a.m.	3 p.m.	6 p.m.	M
Day of operation	800	800	000 2000	3000	100	800	5 150		10 30		53 94	06 440	115	18
3	000		000 (and 5% glucose)				50		20	35	157	4	303	18
4	2000		300 (and 5% glucose)		20		350		10	70	203	55	20	21
5	2000		000 (and glucose)						10		54	80	35	86
6	2000		300 (and 5% glucose)						10	5	56	27	203	50
7	2000		300 (and 5% glucose)						10	266	203	08	60	
8	2000		000 (and 5% glucose)				20		10	74	88	7	18	

*There are no acetone or diacetic acid in the urine.

No evidence of ascites the liver was not palpable and the icterus present before operation had cleared completely. He ingested a 2500 caloric diet daily which included 400 grams of carbohydrate.

The patient died 3½ months after operation. Necropsy revealed abdominal carcinomatosis. No pancreatic tissue was discovered anywhere.

This is the first patient reported with fairly severe diabetes not due to tumor destruction of the pancreas but of spontaneous origin who has been subjected to total pancreatectomy (and total gastrectomy). Following the immediate effects of operation the diabetes was at no time augmented in severity on the contrary there were periods when it appeared less severe than before total pancreatectomy. With the caloric intake equivalent to about 2500 (400 gms carbohydrate) the insulin requirements were 30 units protamine and 10 units regular daily. These observations raise many fundamental questions concerning the nature of diabetes mellitus in man and the exact status of the pancreas in this condition. Detailed data on the various observations made upon the metabolism of this patient following the immediate postoperative period will be published subsequently in greater detail elsewhere. Some data are presented in Table II.

Including the case here reported 5 total pancreatectomies have been performed in this institution for carcinoma. Three of these have been previously commented upon by Goldner and Clark. Although their survival was brief suggestive evidence of relatively moderate insulin requirements in nondiabetic patients following total pancreatectomy was presented. In Fallis' case briefly reported by McClure the insulin requirement in the previously nondiabetic patient after total pancreatectomy was only 26 units a day 4 months after operation. The objectives attained in the case here reported were (a) relief from

TABLE II—LABORATORY DATA—2½ MONTHS AFTER OPERATION

Blood	
Red blood cells	4,250,000
Leucocytes	6,700
	(no recent transfusions)
Plasma proteins, mgm. %	6.64
Nonprotein nitrogen, mgm. %	19.
Serum lipids, mgm. %	977
Bromsulfaleine test—3 mgm. per kgm. 0%	
retention in 30 minutes	
Icteric index	8
Blood amylase	
5 months before operation—units	8
1 week after operation—units	9.
2 weeks after operation—units	10.
8 weeks after operation—units	71

jaundice and (b) resection of all gross evidence of neoplasm within the abdomen *at the time of operation*. The experiences in this patient are recorded again to demonstrate the feasibility of very radical resections for abdominal cancer in encouragement of the extension of radical surgery in the treatment of malignant neoplasms.

SUMMARY

A diabetic patient with carcinoma of the body of the pancreas that had extended to

adjacent viscera, successfully underwent total pancreatectomy total gastrectomy splenectomy total duodenectomy and left adrenalectomy. The diabetes was not aggravated following the operation; there were periods when, under the conditions of observation, the diabetes appeared to be less severe than before operation.

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PANTOPAQUE MYELOGRAPHY AS AN AID IN THE PREOPERATIVE DIAGNOSIS OF PROTRUDED INTERVERTEBRAL DISCS

A Preliminary Report

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THE following report is intended to emphasize the fact that if the unilateral exploration is carried out for protruded intervertebral disc without preoperative myelography (1, 3) or multiple (2) preoperative myelograms as well as certain other intradural lesions (8) may be overlooked.

Myelography has been largely abandoned by some surgeons in the diagnosis of herniated disc. This has been done on the basis that clinical diagnosis is sufficiently accurate and also because the older contrast media were deemed unsatisfactory. The objection to the use of air (or oxygen) have been that it frequently fails to show the presence of a small disc protrusion and that severe headache may temporarily follow its use. Lipiodol was used with caution because it could not be easily removed from the subarachnoid space and if left *in situ* might give rise to intradural irritative phenomena. Thorium dioxide solution (thorotrast) is radioactive and an irritant.

The new contrast medium pantopaque (ethyl iodophenylundecylate) (6, 10, 11) has now made myelography a simpler and more justifiable procedure than it was in the past. Spurling and Thompson, who have been using this method routinely in all suspected disc cases, report very accurate interpretations. They point out that the exact level of the lesion may be localized and operation limited to exploration at the precise interspace. This seems preferable to operative exposure at two levels which is sometimes necessary before the protruded disc is found. In addition it may be recalled that Camp reported (12) per-

cent of protruded intervertebral discs in my experience have been multiple (2).

Unfavorable reactions are to be expected from the use of pantopaque if the agent is removed immediately following the examination. Removal can almost always be accomplished in this case by aspiration through a 20 gauge needle as described by Kubik and Hampton. If for any reason the agent is not removed it does not give rise to any greater reaction than does lipiodol and in time is apparently largely if not wholly absorbed.

In the present study 36 pantopaque myelograms were done on patients with symptoms simulating those seen in the presence of a unilateral herniated nucleus pulposus. Pathognomonic signs and symptoms were not present however in all cases. In the roentgenoscopic and roentgenographic examination a filling defect in the pantopaque shadow typical of a herniated disc was demonstrated in 20 cases and in 14 of these the diagnosis was verified by one of us (F. A. E.) at operation. The other 6 individuals were not explored as their condition existed prior to induction into the Army. Fourteen patients had negative myelograms. In this small series it is interesting that 2 patients had large bilateral filling defects and 2 others had evidence of diffuse intradural pathology considered to be probably arachnoiditis.

Of the 2 patients in whom myelography showed bilateral filling defects in the lumbar region one was explored (Fig. 1) and an unusually large protruded disc was removed from the fourth interspace on the left and also a large one from the fifth interspace on the opposite side. At each level the nerve root was



Fig. 1 Large filling defects in the column of pantograph are evident, one in the fourth lumbar interspace on the left side and the other in the lumbosacral junction on the right indicated by the arrow. At operation 1 herniated discs were removed one from the site of each filling defect. Clinically this patient presented signs and symptoms of protruded disc only on the left side.

Fig. 2 Here seen bilateral filling defect in the fourth lumbar interspace probably due to herniation of disc or hypertrophy of the ligamentum flavum on both sides. Denotes the bilateral nature of the pathology; the patient's symptoms suggested only unilateral lesion. b The pantograph has been removed except for one droplet in the sulcus sac.

markedly compressed. It is noteworthy that before operation the patient had symptoms suggesting a herniated nucleus pulposus only on the left. His pain had always been referred from the lumbar region to the left leg. The ankle jerks were present but the left was less active than the right. In this case a clinical diagnosis of protruded lumbar disc on the left was made. With such a diagnosis it seems obvious that without the aid of myelography the usual unilateral exploration would have been carried out and the herniated nucleus pulposus removed only from the fourth interspace on the left. A similar pathological lesion present at the lower level on the right would have been overlooked and recurrence of symptoms on this side would have been very likely. The other individual in whom a bilateral filling defect was present likewise had symptoms suggesting a herniated disc only on the left. Following an injury to his back in 1940 he had complained of low back pain with sciatic radiation to an area just above the left popliteal space. This had occurred in increasingly se-

vere attacks. Anterior flexion of the lumbosacral spine was limited. The pain was aggravated both by coughing and anterior flexion of the spine. Straight leg raising was strongly positive on the left at 40 degrees and the left ankle jerk was diminished. Myelography revealed a large bilateral filling defect at the fourth lumbar interspace which had the appearance of a bilateral protruded intervertebral disc or possible bilateral thickening of the ligamentum flavum (Fig. 2). This patient was not operated upon because his condition developed before entering the Army. It seems apparent however that if operation had been undertaken on clinical grounds alone this would have been restricted to a left unilateral exploration and the pathological lesion on the right side would not have been found.

With reference to the two individuals showing evidence of diffuse intradural pathological lesions, probably arachnoiditis, the clinical diagnosis of unilateral protrusion of a lumbar disc was made in each case on the basis of a competent neurological examination. The first



Fig. 3. (left) Normal pantopaque myelogram at fifth lumbar interspace. (right) Normal pantopaque myelogram at fifth lumbar interspace.

Fig. 3. (left) The pantopaque is diffusely scattered throughout the lumbar canal and is broken up at different levels, indicating the presence of a diffuse intralumbar pathological lesion (see text). Clinically the patient had presented signs and symptoms of a unilateral herniated lumbar disc.

Fig. 4. Note the diffuse breaking up of the normal pantopaque column into globules. This is a contrast film taken throughout the lumbar canal. This film was taken with the patient in the erect position (see text). A clinical diagnosis of herniation of a lumbar disc had been made in this case.

about 45 degrees from the vertical and straight leg raising was very painful at 60 degrees on the left. There was a narrow strip of diminished sensation to pin prick over the anterolateral aspect of the left calf of the leg. The knee and ankle jerks were all sluggish and no difference between the two sides could be elicited. The patient had had no abnormal symptoms in the right leg. The myelographic findings were very similar in the above 2 cases (Figs 3 and 4). At roentgenoscopic examination the pantopaque in both patients did not remain a compact column as it usually does when moved from level to level by tilting the table. On the contrary it became hung up into large globules at different levels and passed very slowly from level to level not as a column but in fine multiple trickles or strands. This type of abnormality was found in both patients to extend at least from the first to the fifth lumbar interspaces. The first patient described herein who presented this picture (Fig 3) was explored. A partial laminectomy was performed at the fifth lumbar interspace and the dura was opened. The arachnoid was not transparent but faintly grayish and many fine subarachnoid adhesions were noted binding together the roots of the cauda equina. The interspaces at the fourth and fifth levels were explored on the left side and no herniated

patient had a history of low back pain of 4 months duration with sciatic radiation down the posterior aspect of the left thigh lateral aspect of the calf of the leg and irregularly over the foot. Coughing aggravated the sciatic pain. There was marked splinting of the lumbar erector spinae muscles. Straight leg raising was very positive on the left at 20 degrees. The left ankle jerk was diminished and there was hypalgesia to pin prick over first sacral on the left anterolateral portion of the calf of the leg. There had been no symptoms referable to the right leg. The second patient gave a history of a fall 2 years previously at which time a diagnosis of a fractured sacrum was made. This was followed immediately by low back pain and later by pain which radiated down the posterior aspect of the left thigh to its lower third. There had been repeated exacerbations of the symptoms. Anterior flexion of the lumbosacral spine was limited to

disc was found. It was our opinion that surgical intervention was unnecessary on the other patient as the diagnosis of a diffuse lesion probably arachnoiditis (Fig 4) was apparent and it seemed doubtful if operation could give relief.

Myelographic studies in these 2 cases demonstrated to us that our clinical diagnosis of unilateral protrusion of a nucleus pulposus was erroneous. If the clinical findings alone had been relied upon a negative exploratory operation would have been done in both cases.

In addition to diffuse intradural lesions there are of course other pathological conditions which may simulate a protruded disc such as a small meningioma or perineural fibroblastoma (5, 7). Examination of the spinal canal by use of pantopaque will usually reveal such conditions.

Of the 36 cases reported it was mentioned that in 14 of these no abnormality was noted in the myelogram. We agree that a normal appearing myelogram does not rule out a herniated disc nor a concealed one and in such cases it is our opinion that one must rely upon the clinical picture in determining whether or not operation is indicated.

A word of warning should be added concerning the indiscriminate use of myelography in the diagnosis of herniated disc. It is believed that such a procedure should be carried out only in those cases in which a protruded intervertebral disc is suspected on the basis of a detailed history and careful neurological examination. The myelographic study should be performed by those familiar with the procedure and qualified in its interpretation and wherever possible in the presence of the surgeon who is to operate upon the patient.

SUMMARY

The findings in 36 pantopaque myelograms performed on patients suspected clinically of

having a unilateral protrusion of a nucleus pulposus at a low lumbar level are reported. In 2 of these patients myelography indicated the presence of bilateral protrusion of a disc, which in one case was at two different levels. In 2 of the other patients, diffuse intradural pathology probably arachnoiditis, was demonstrated.

It is believed that these findings illustrate the unreliability of a diagnosis based on clinical signs and symptoms alone. Clinical criteria indicated the presence of a unilateral herniated disc in each case and if relied upon would have failed to reveal the presence of a herniated disc on the opposite side or an intradural pathological lesion.

If errors in diagnosis are to be reduced, it is therefore advocated that before a patient is subjected to operation, pantopaque myelography be carried out in those cases suspected of having a herniated nucleus pulposus in the lumbar region.

Pantopaque as an agent for use in myelography has few of the objections found with those used in the past.

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MALARIA FROM BANK BLOOD TRANSFUSIONS

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THE return of military personnel from malaria infested areas to the continental United States increases the possibility of the transmission of the disease by blood transfusion. This accident has been comparatively rare if one judges by the number of reported cases. In 1938 Wright was able to collect only 23 cases from the literature but could add 6 of his own. Gordon found 5 more case reports and described the first recorded instance of the production of malarial infection from the use of stored or bank blood. We wish to report 2 patients, who were infected with blood which had been refrigerated for 5 days.

CASE 1: H. F., a white woman aged 57 years, fell on November 11, 1940, and sustained an intracapsular fracture of the left femur. She was admitted to another hospital where the fracture was reduced and plaster fixation was applied. Two months later malposition and nonunion were noted and she was transferred to the Henry Ford Hospital for the insertion of a Smith-Petersen nail. This operation was performed on January 24, 1941, by Dr. C. L. Mitchell. During the open reduction 600 cubic centimeters of citrated blood from the bank was transfused.

On the first postoperative day there was a temperature elevation to 101 degrees. She was afebrile during the 2d, 3d, and 4th weeks. On the 32d day she had a fever of 101 degrees and again on the 35th day the temperature was 100.6 degrees. No chills were recorded. Because the second bout of fever promptly subsided and the patient was without symptoms, she was discharged.

Two weeks later she was readmitted to the hospital. She stated that since returning home, she had had attacks of nausea and vomiting preceded by chilliness and sometimes actual shaking. There was a feeling of weight in the stomach and marked anorexia. The chief physical finding was the presence of tenderness and muscle spasm in the right upper quadrant. A medical consultant suggested that she might have a penetrating peptic ulcer, cholecystitis, or pancreatitis. The red blood cell count was 3,100,000 per cubic millimeter, white blood cells 3,350 per cubic millimeter, 67 per cent polymorphonuclears. Roentgen examination of the abdomen was reported as showing probable enlargement of the spleen. The significance of this observation was not immediately appreciated.

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On March 16, the 2d day of the second admission there was a chill and a fever of 105 degrees. A smear for malarial parasites on March 17 showed some inclusion bodies not typical for the protozoa. The next day typical organisms were seen and the diagnosis of quartan malaria was established. Quinine hydrochloride was given in 10 grain doses 3 times daily after March 20. Two days later the temperature was 99 degrees and it remained normal during the rest of the period of hospitalization.

The blood bank records showed that the patient had received blood which had been on hand for 5 days. The donor was a volunteer who had repaid the debt of his wife's nephew who had just had a resection of a segment of intestine for regional enteritis. He was 50 years of age, born in Sicily. He had lived in Michigan since he was 16. At the time of the blood donation he indicated to the questioner that he had not had malaria. However, follow-up inquiries revealed that he had had chills and fever for 4 months when he was 10 years old. He had been perfectly well for 25 years. On one occasion after the transfusion in question an ordinary blood smear was negative for malarial parasites.

CASE 2: A. M., a white woman aged 23 years, was found to have bronchiectasis of the right lower and middle lobes. On May 7, 1942, the involved lobes were removed at one stage by one of us (C.R.L.). During the operation 500 cubic centimeters of citrated bank blood were given. Her postoperative course was very satisfactory. She was afebrile from the 3d to the 22d day, at which time she was given a second transfusion on account of the presence of slight secondary anemia. Following the transfusion there was an immediate temperature elevation to 101.6 degrees, but the next day she was afebrile. She was discharged on May 30 with instructions to keep a temperature chart.

On June 3 there was a fever of 101.6 degrees. On June 16 she reported that she was having chills and fever every 3d day. A smear for malarial parasites taken on this day was negative. On June 24 she stated that she had had no fever since the last visit. On July 5 the temperature was 104 degrees and every 3d day thereafter until July 15 she had chills, fever, vomiting and headache. The chills started between 4:00 and 6:00 in the afternoon and lasted 5 to 6 hours. Examination of the blood at this time showed typical quartan parasites. The spleen was

definitive treatment the thoroughness and extent of wound revision and débridement are the determining factors in early and late wound infections and above all else prove that sound surgery is the essential factor in clean wound healing. From collateral experience with established infections we know that the sulfonamides prevent the generalized spread of infection caused by susceptible organisms especially the hemolytic streptococcus and from this experience we may assume that they do so when used prophylactically. This would seem to be further supported by the low mortality in the series presented here. Whether they prolong the period between contamination and invasion of tissues by bacteria we can only surmise. But in preventing local infection in civilian wounds these studies do not show that the sulfonamides used locally or systemically give any better results than in wounds treated with the same surgical care but without the drugs. They are therefore only an adjuvant to the treatment of infections in wounds and are in no sense a substitute for sound surgery.

Some of the committee feel that it may be expecting too much to hope that any drug will ever be discovered which will possess such a selective action on bacteria as to destroy them completely in a wound without at the same time causing serious injury to the tissues and leucocytes. Bacteriostatic agents like sulfonamides are not markedly injurious to tissue but cannot be expected to destroy completely the contaminating bacteria. In the field of antibiotics something may yet be found and should be searched for. When the adjustment of the factors in the wound is such as to permit healing with a minimum amount of disturbance of the blood supply and with a comparatively minor destructive phase the use of bacteriostatic agents might be of some

value. However in most wounds which are subject to closure the effect of the drug is not of sufficient magnitude to permit total destruction of organisms by drug and phagocytes, and any foci of tissue necrosis usually become foci of bacterial growth. This conclusion points up in the most convincing way the primary importance of sound surgical methods in the management of wounds and assigns a relatively minor position to the use of the bacteriostatic agents so far available.

Because of the differences in conditions in civilian casualties as compared to those in war zones, no comparisons are made nor is any recommendation made for the use or disuse of bacteriostatic drugs as prophylactic agents in the prevention of local wound infection in war wounds. But it is the opinion of this committee that these agents should be used to prevent systemic invasion of infection. It is finally the unanimous opinion of the committee that as always the carrying out of the sound surgical principles of preventing and treating shock of hemostasis of removing nonviable tissue and foreign bodies, of repairing the wound with minimum tissue tension of maintaining maximum nutrition to the tissues, of immobilization of the wounded part—in other words, sound surgery is the *sine qua non* of wound therapy.

Only those who have observed the work of Dr. Meleney and his associates in collecting and analyzing the data from the several units submitting reports of their results, can appreciate the untiring and honest effort that has gone into this report. As the results of other investigators in this country, Canada, and England working with the sulfonamides in the prevention of wound infection accumulate they are corroborating the findings in this report, and the essential rôle assumed by sound surgery.

THIS is the report of the Statistical Summary for the Study of the Prevention of Infection in Contaminated Wounds and Burns under Contract OEMCmr 85 for patients admitted to the unit hospitals from January 1, 1942 to October 31, 1943. Fifteen hundred of these cases

studied up to April, 1943, were briefly reported in an article which appeared elsewhere.

GENERAL CONSIDERATIONS

A. The make up of the study units. Nine units have contributed to this study over a

period of 22 months and the results presented herewith are based on 2 191 complete records of cases. These units were set up at the Akron City Hospital the Charity Hospital in New Orleans the Cincinnati General Hospital the Cook County Hospital in Chicago the Detroit Receiving Hospital the Henry Ford Hospital in Detroit the Johns Hopkins Hospital in Baltimore the Massachusetts General Hospital in Boston and the Presbyterian Hospital in New York. Two of these units namely the Cook County Hospital and the Henry Ford Hospital have limited their study to burns. Three of the units discontinued the prophylactic study after the first year the leader of one group entering the armed forces to carry on investigative work in surgical infections. The two other units turned to a study of established infections. Four units continued the study of all three categories—soft part wounds compound fractures and burns throughout the whole period of study and are continuing the project with the addition of three more units studying compound fractures and two more studying burns under a modified plan which will be reported later.

The steady withdrawal of personnel to active war service from the units both in the clinic and in the laboratory has made it increasingly difficult to maintain the high standards originally set for the completeness of the records and the promptness of reporting the cases to the central office. The curtailment of automobile traffic has materially cut down the incidence of civilian accidental injuries so that the total number of cases is considerably less than was anticipated at the initiation of the study. However the consistency of the results as they have been tabulated and reported every 2 months lends weight to their significance.

B The nature of the material. Hospitals were chosen which had available or could obtain a fair number of serious civilian accidental wounds particularly from severe automobile or industrial accidents. It was recognized that civilian accidental wounds differ from war wounds in certain respects and any conclusions that may be drawn from them must be applied to war wounds with some reservations. The three most important dif-

ferences are (1) the wide range of age and general condition of the civilian patient and the narrow age range of the soldier and his good general condition (2) the relatively short interval between accident and operation in the civilian cases and the wide range of time interval of the soldier's wound (3) the relatively short and atraumatic transportation of the civilian case from the scene of the accident to the hospital and the wide range of trauma to the wounded soldier during this period.

The first of these three differences would favor a high incidence of infection for the civilians. The other two would favor a high incidence of infection for the soldier. Other differences which might be considered are the relatively uniform method of treatment in the civilian hospitals in this civilian study the compromises that must be made in the operative procedure on the soldier because of the flood of cases in a big push the high velocity of the traumatizing agent of the soldier the wider variations in the degree and kind of bacterial contamination of the soldier's wound because of injuries received under different climatic conditions on land on sea and in the air. Furthermore many soldiers will have had drug applied to their wounds over a varying period of time between the infliction of the wound and the definitive treatment. Observations on civilian cases under similar conditions would be most difficult to obtain. Of the cases included in this report it may be said in general that the burns of the civilian are most comparable to the military casualties the compound fractures are next and the soft part wounds are least.

In spite of these differences it might be possible to select from these civilian cases groups which are strictly comparable with the wounded combatant but first we would have to obtain as complete data from a group of wounded soldiers. All of these points clearly indicate the complexity of the problem and the necessity for setting up a well controlled study in combat areas in which careful records can be kept of all of the relevant factors in each case which would favor or minimize the development of infection. It has been repeatedly urged by the Subcommittee on Surgical Infections and by the General Surgical

tion In his discussion of the problem he writes as follows particularly with regard to the comparability of the controls with drug treated cases

Speaking generally if a group of controls and a treated group should show the same distribution with respect to all apparently relevant items it might not be unfair to compare the gross results. Here, however, we find that the two groups do show a rather marked difference with respect to some factors so that the gross comparisons are not completely valid. Furthermore even should the two groups be distributed somewhat to the same extent on the bases of the factors listed here in the tables of crossclassification that would not insure that they were equitably distributed with respect to other factors. Admittedly if the two groups seem to be equitable with respect to a large number of possible factors they might be compared with some degree of assurance.

In our case it seems that one way out of the difficulty is not to rely on the gross comparisons but to make the comparisons of the drug and control series specific for a group of factors apparently important in the determination of infection singly or preferably simultaneously. Thus for example, we may compare the control and drug specifically for a given amount of tissue damage and a given amount of contamination simultaneously since these two factors appear to be relevant in the subsequent course of wound healing. This gives us a number of comparisons instead of one gross comparison. The controls and treated cases with given grade of both factors may still not be completely comparable with respect to other factors such as wound area, distribution with respect to units etc. but they are quite apt to be far more comparable with respect to the factors than were the original two series *in toto* and certainly they are comparable with respect to the two factors considered. One more factor worked in to a crossclassification scheme would insert a further element of comparability and render even further removed the possibility of consistent heterogeneity running through all the comparisons. Again, the more intensive the crossclassification the smaller the frequency in any particular subgroup, with the result that individual comparisons will have little merit *per se* because of the tremendous magnitude of chance errors. In such cases of course, reliance cannot be put on any particular specific comparison but rather on the series of comparisons as a whole.

This advice has been followed and although gross comparisons have been made on Tables IV (soft part wounds) and XXXIII (compound fractures) emphasis has not been placed upon them but attention has been focused on the comparisons of drug treated

cases with the controls in groups having one, two or three common factors which seem to be related to wound infection.

Wherever possible the formulae of the biostatisticians have been applied to the percentage figures. The formula generally used has been that which was recommended for surgeons by Campbell in his article¹ entitled

The Statistical Method.

The formula indicates whether or not percentage differences are statistically significant, minimizing the element of chance. The results are the same whether the figures are given for the percentage of infection or the percentage of clean wound healing. Inasmuch as this study is directed toward lowering the incidence of infections, the figures for infection have been used in the accompanying tables. Significant differences have been indicated by the letter S.

Where complete data have not been available in any given case so that the totals do not reach the sum total of cases in any group this has been indicated by an asterisk. For one reason or another certain of the relatively unimportant factors were occasionally omitted from the records.

G The surgical care of the patients. In setting up the study units the difficulties of obtaining well trained personnel was recognized. Many of the clinical surgeons and laboratory workers originally chosen in June of 1940 were called away to active military service in the course of the 18 months of delay in starting the project.

With regard to the surgical care of the patients, no attempt was made to straight jacket the surgeons beyond the requirement that all of the patients were to be treated as surgical emergencies and were to be operated on as soon as it was physically possible with as complete a removal of the dead or injured tissue as the severity of the accident indicated. For this procedure we have used the term *débridement*. Furthermore the patients were to be treated with all of the modern methods at the disposal of the units for the care of shock and other operative and postoperative sequelae and complications associated with such cases.

H The bacteriological studies An attempt was made to work out a complete bacteriological analysis of the tissue removed from the wound at the time of the primary operation. It has been difficult at times to separate out from a mixed flora all of the species present and obtain them in pure culture. The usual methods of wound culture, namely rubbing a cotton swab on the wound surface and incubating it aerobically in broth or even snipping bits of tissue and culturing them aerobically and anaerobically are obviously not enough. An accidental wound is contaminated by bacteria carried in for the most part on foreign bodies which are scattered here and there throughout the wound. A knowledge of the potential agents of infection can be obtained only by taking all of the material removed at débridement and recovering representative members of all contaminating species. This means of course that the bacteriologists concerned must have some knowledge of the whole range of bacteriology both aerobic and anaerobic, and pathogenic as well as nonpathogenic, for almost any kind of organism may contaminate a wound.

Realizing the probable limitations of the laboratory personnel which would be available it seemed advisable not only to have standard procedures and uniform media and an acceptable nomenclature for all of the units but also to set up a central laboratory with a recognized authority in charge to whom all of the difficult problems which might arise could be referred. Further details of this plan and the degree of success obtained will be the subject of a supplementary report prepared by Dr. Ivan C. Hall, the director of the Central Laboratory which was set up in New York at the College of Physicians and Surgeons.

We ordinarily think of different species of bacteria as being pathogenic or nonpathogenic but these are not absolute terms. There are many nonpathogenic strains among a pathogenic group such as the beta hemolytic streptococci and the establishment of infection in a wound depends not only on the number and virulence of the organism but on the conditions of local and general defense present in or developed by the body at the site of the bacterial contamination. This has been amply

confirmed by the present study. In many cases so called pathogenic species have been cultured from the débrided tissue which never gave rise to clinical infection and at the same time some cases developed infection in which only nonpathogenic organisms were originally found. This does not mean that the organisms are not the essential elements of infection but (1) that there are other important factors concerned in the development of infection (2) that there are antagonisms as well as synergisms among the bacteria entering a wound (3) that there are opportunities for secondary contamination from the environment of the patient, and (4) that there are limitations to the knowledge of even the most expert bacteriologist.

In the analysis of the bacteriological data it seemed to be important to show the relationship between the development of infection and the incidence of various organisms in the débrided tissue as well as in later wound cultures with particular reference to the treatment which the case received.

Those cases have therefore been taken as separate groups in which the hemolytic streptococcus or coagulase positive Staphylococcus aureus or other coagulase positive micrococci or pathogenic gram negative bacilli or Clostridium welchii or anaerobic streptococci were found in the débrided tissue. The number of these cases in which clinical infection developed has been noted. The number of these cases in which these organisms persisted and likewise the number of cases in which they were found later during the course of wound healing although not found in the original cultures of the débrided tissue have been determined. Each of these groups has been further subdivided according to the local and general chemotherapy which they received in order to find out whether the drugs were able to help the body rid the wound of the original contamination or prevent the later establishment of organisms secondarily introduced.

I The definition of infection Attention has been focused upon the process of wound healing with particular reference to the development of infection. This has been defined as the reaction of the tissues in and about the

TABLE III — MAJOR FACTORS CONCERNED WITH WOUND INFECTIONS

	Totals	Per cent infection			
		None	Serious	Trivial	Total
Multiple wounds	300	5.8	7.7	5.15	8.44
Single wounds	876	2	2	8.8	3
Stab wounds	172	4.2	5.6	10	4
Gross or gross contamination		74			5
Lesser gross contamination	60	8	5		3
Greater tissue damage			5	5	3
Lesser tissue damage	104	2	6	5.6	
Operation after hours	95		5		
Operation before hours	65	6			5
Large area				5	5
Small area				5	5.5
Incomplete débridement	70	74	6	6	5
Complete débridement	607	74	5	5.6	5
Incomplete removal of foreign body	70*				8.4
Complete removal of foreign body		2	6		3
Irrigation for over 10 minutes	30		6	5.5	5.7.4
Irrigation for less than 10 minutes			5.7	6	5.8
No closure of wound	74	5	5.6.7	5.10	5
Complete closure of wound	39		5.5	5	5
Partial closure of wound	7	54		9	40.2

5. Statistically significant differences
 1 certain cases these data are not recorded
 *Some stab wounds were single and some multiple

breakdown of our efforts to prevent the activity of the contaminating organisms.

The variability of the results in the different units is probably chiefly indicative of the variability of the material and the conditions found in the different hospitals but the possibility that there was some degree of difference of interpretation of the terms serious and trivial infections cannot be denied in spite of the frequent discussions on this point at the meetings of the committee.

Even for those units having an appreciable number of controls, the difference of per cent infected between drug treated and controls is at variance. Such variations do not invalidate the results but emphasize the importance of the statement made in the introductory paragraphs that in order to arrive at reliable conclusions the experience of all of the units has

TABLE IV — SHOWING THE RESULTS IN SOFT PART WOUNDS OF CLOSURE WITH AND WITHOUT TENSION

	Wound classes		
	With tension	Without tension	Not recorded
Complete closure			
Total		195	
Per cent serious infections	5	14.0	5
Per cent trivial infections	5	16	8
Partial closure			
Total		15	
Per cent serious infections	5		5
Per cent trivial infections	5		5.8

5. Statistically significant differences

to be pooled and then regrouped according to the presence or absence of relevant factors. Thus the only safe comparisons must be drawn from the series of differences emanating from crossclassifications.

Table III takes the group as a whole and divides it into either two or three subgroups to bring out some of the chief factors associated with infection. It is seen that there is a high incidence of infection in multiple wounds as compared with single wounds in wounds which had greater gross contamination as compared with those with lesser gross contamination in those with greater tissue damage as against those with lesser tissue damage in those operated on later than 3 hours as contrasted with those operated on within that period in large versus small wounds in those with incomplete as against those with complete débridement in long versus short irrigation and in partial closure of the wound as compared with complete closure or no closure. In most of these categories we have confirmed statistically what we have learned from clinical experience regarding the main factors concerned with the development of or resistance to infection. It is of interest to note that significant differences in the total percentage of infection are found in all but one of these listed here. These differences are either in the serious infections or in the trivial and sometimes in both. Many other factors have been analyzed but seem to be less important,—for example shock drainage of the wound and involvement of the peritoneal cavity and the

TABLE V — INCIDENCE AND PERCENTAGE IN SOFT PART WOUNDS OF SERIOUS AND TRIVIAL INFECTIONS IN THE CONTROLS AND IN CASES OF PATIENTS WITH THE VARIOUS FORMS OF DRUG TREATMENT

	Cases	Number of infections			Per cent of infection		
		Serious	Trivial	Total	Serious	Trivial	Total
Total number of cases	976	59	4	63	6		7.6
Ketlet general (or local) sulfonamide	3	3	5	40	4.7	7.8	5
Total sulfonamide	604	44	79	3	7.3		5.30
General without local	53	5		7	9.8	7.8	7
General (with local) sulfonamide and sulfathiazole	87	8	5	34	4	5.0	5
General with local sulfonamide	5	20	20	20	8.0	7.4	26
Miscellaneous sulfonamide	30			3	6	5	7.7

S Statistically significant differences.

TABLE VI — PERCENTAGE IN SOFT PART WOUNDS OF CASES IN DRUG TREATED PATIENTS AND CONTROLS WHICH HAD THE MAJOR FACTORS FAVORING WOUND INFECTION

	Totals	3 Controls, per cent	Totals	604 Sulfonamide, per cent
Greater contamination	3	3	0	36
Greater tissue damage	5	30.4	20.8	40.5
Operation after 4 hours	38	0	96	6
Incomplete débridement	5	78	24	2.8
Prolonged irrigation	5	57	7.7	24.6
Large wound area		49	5	90
Partial closure of wound	5	9	8	63

S Statistically significant differences

Table V takes the group as a whole (with out regard to the factors favoring infection) and divides it into controls and the three main categories of drug treated cases together with a small group of miscellaneous drug treatments

This table shows that the results in the three main categories of drug treatment yielded no significant differences. The very small series of miscellaneous treatments shows a significantly smaller number of infections but for various reasons these cases are not comparable with the others and one cannot conclude that the miscellaneous drug treatments are any better than the three regularly employed. This similarity of the three main drug groups runs through all of the cross tabulations and it seems to be of particular interest that the combined general and local use of drug is no better than the systemic administration alone. With no difference in results shown between the three methods one can therefore in the subsequent tables to be presented pool the whole drug treatment experience and consider it against the control experience. This comparison seems to indicate that the control patients did significantly better than the treated patients with a total of 12.4 per cent of infections as compared with 20.4 per cent among the drug treated patients. Does this mean that the drugs did more harm than good?

To consider this point one has to know whether the controls are strictly comparable

alimentary tract. All of these groups need further breakdown for other factors play important rôles in each of these categories which may weight the figures one way or another so as to disturb the comparability of the main groups. For example one might expect the group with prolonged irrigation of the wound to include a larger number of cases with maximum gross contamination than the group with a short period of irrigation so these groups must be subdivided and cross tabulated.

Table IV shows a cross tabulation between closure of the wound and tissue tension. In some of the earlier cases this factor was not recorded. It is apparent that tension or the conditions which led to its use with both the partial and complete closure of wounds after débridement, played an important rôle in the development of infection but we can find no evidence that the use of sulfonamide modified this result in any way. It is to be noted that the incidence of infection is higher in the partially than in the completely closed wounds. This suggests not only that these wounds were exposed to secondary contamination but that partial closure was a compromise with infection, possibly done only when it seemed necessary to cover up important structures.

TABLE VII — INDICATING THE SEVERITY OF THE INJURY BY THE DEGREE OF PENETRATION OF THE WOUND OF SOFT PARTS WITH PARTICULAR REFERENCE TO THE INCIDENCE OF INFECTION IN CASES OF DRUG TREATED PATIENTS AND IN THE CONTROLS

	Controls			Sulfonamide cases		
	Totals	Per cent infection		Totals	Per cent infection	
		Serious	Trivial		Serious	Trivial
Rin and subcutaneous tissues only	51		9.8	60		5.3
Muscles or tendons	8341	5	7.5	405	6	3
Nerve injury	837	7	8	208	6.3	6
Serous cavity	8	3	6.3	9	30	10
Joint cavity		20		20	1	3
Respiratory tract		00	00	00	5	8
Alimentary tract	8	80	00	00	8	17
Urinary tract		00	00	00	23	00
Heart or great vessels		00	00	00	3	3
Brain or spinal cord		00	00	00	00	30
Other sites	00		3	00	8.7	1.7

*Many of these cases duplicate others.
 † Statistically significant difference.

TABLE VIII — SOFT PART WOUNDS: COMPARISON OF CASES IN DRUG TREATED PATIENTS AND CONTROLS WITHIN SUBGROUPS COVERING FIVE OF THE MAJOR FACTORS CONCERNED WITH WOUND INFECTION

Major factors	Controls			Sulfonamide cases		
	Totals	Per cent infection		Totals	Per cent infection	
		Serious	Trivial		Serious	Trivial
Gross contamination		8	10.7	18.5	9	3
Lesser gross contamination	4		6	6	38.5	
Drainage damage		7	6	9.7	20.6	8.7
Lesser tissue damage	8	0.9	4	20.6	1	10.5
Incompleteness of debridement	4	10	7		8.6	5
Complete debridement	5		8	10	13	6
Irrigation more than				8	26	9.6
Irrigation less than	20.5		10	19	4	10
Early operation more than 4 hrs	10*	3		26	3	10
Early operation less than 2 hrs	8.7	3.3	7	20.6	20.1	1.7

*Data missing in 1 of these cases.
 † Statistically significant difference.

as a group with the drug cases, with respect to those factors which tend to favor infection as indicated on Table III. Table VI shows the percentage of several of those factors in each of the two groups. It is seen that drug treated cases included a higher percentage of each of those factors than the controls. Several of these percentage differences are statistically significant and the others are not but all point in the same direction and seem to indicate that the controls as a group were somewhat less serious. One cannot tell from the figures whether or not these differences with regard to severity completely offset the differences in the infection percentages of the two groups seen in Table V.

These two tables (V and VI) which point in different directions clearly illustrate the point made in the preliminary paragraphs—that gross comparisons may lead one astray and they emphasize the necessity for making comparisons within groups having one or more

common factors. Cross tabulations have been carried out for this purpose and appear on Tables VII, VIII, IX, and X.

Some idea may also be gained of the severity of these accidental wounds by a study of Table VII which indicates the depth of wound penetration with relationship to the drug treatment. The early impressions that the sulfonamides were of particular value in serous cavities—particularly in the peritoneal cavity which has been soiled by intestinal organisms, led to their more frequent employment in these areas. In the whole study the ratio of drug treated cases to the controls is about 2 to 1 but in some of the categories shown in Table VII it is 5 to 1 or even 10 to 1. Nevertheless this offers an opportunity to compare the drug treated cases and the controls in groups in which a common factor is operating. In this table there are many duplications. Most of the wounds involved consid-

TABLE IX.—SOFT PART WOUNDS COMPARISON OF CASES IN DRUG TREATED PATIENTS AND CONTROLS WITHIN SUBGROUPS CONTAINING TWO COMBINED MAJOR FACTORS WHICH ARE CONCERNED WITH WOUND INFECTION

Major factors combined	Controls			Sulfonamide cases		
	Totals	Per cent infection		Totals	Per cent infection	
		Serious	Trivial		Serious	Trivial
Greater contamination and greater tissue damage	66	7.6	1.6	54	3	6.9
Greater contamination and lesser tissue damage	37	8	3.4	35	7.7	8
Lesser contamination and greater tissue damage	6	6.6	1	44		4.6
Lesser contamination and lesser tissue damage	5	18	0	6.3	24	3
Greater contamination and irrigation > 10 min.		3.6	.8	15.4	74	10.8
Greater contamination and irrigation < 10 min.	8	6	7.4	3.6	45	7
Lesser contamination and irrigation > 10 min.	38	9	4	14.3	7	8.3
Lesser contamination and irrigation < 10 min.	8	84	2.3	8.4	8.7	2.2

§ statistically significant differences.

erably more than just the skin and subcutaneous tissues. Nerves and tendons were frequently involved together and muscles were injured along with most of the serous cavities. The infection figures reveal in every category a higher percentage in the drug treated cases than in the controls and several of these differences are statistically significant. It is of interest also that among the controls there were 8 cases involving the alimentary tract without an infection among them.

In Table VIII the cases are divided in such a way that the drug treated cases and controls can be compared within subgroups featuring certain factors which are thought to be of major importance with respect to the development of wound infection. It is seen that in every category with one close exception in the smallest group the total percent

TABLE X.—SOFT PART WOUNDS COMPARISON OF CASES OF DRUG TREATED PATIENTS AND CONTROLS WITHIN SUBGROUPS CONTAINING THREE OF THE MAJOR FACTORS COMBINED WHICH ARE CONCERNED WITH WOUND INFECTION

Major factors combined	Controls			Sulfonamide cases		
	Totals	Per cent infection		Totals	Per cent infection	
		Serious	Trivial		Serious	Trivial
Greater contamination, greater tissue damage and incomplete débridement	3	30.7	5.4	46	53	5
Lesser contamination, lesser tissue damage and complete débridement	5	0.7	0.0	3.7	3.7	45
Greater contamination, greater tissue damage and irrigation over 10 min.	8	3.6	27.8	33.4	64	10.9
Lesser contamination, lesser tissue damage and irrigation less than 10 min.	5	40	0	1	43	9.5
Greater contamination, greater tissue damage and operation after 3 hours	6	6.7	13.3	20	30	3.3
Lesser contamination, lesser tissue damage and operation before 3 hrs.	8	20	4	1	5.7	20.5

§ statistically significant differences

age of infections was higher in the drug treated cases than in the controls. In all but one instance in each this held true for both serious and trivial infections. It will be noted throughout the table that the number of cases with factors favoring infection are smaller than those without those factors in both the drug treated series and the controls. This may be an indication that these civilian cases are as a whole group less serious injuries than might be available for a study among wounded soldiers. When the biostatistician's formula is applied to the figures in this table it is seen that the difference between the figures for the controls and the drug treated cases is statistically significant and in favor of the controls only for those cases in which the factors favoring wound infection is minimal. However in the

TABLE XI—SOFT PART WOUNDS DAY OF ONSET OF SERIOUS AND TRIVIAL INFECTIONS CORRELATED WITH THE DRUG TREATMENT AND WITH THE CONTROLS

	Not recorded	Control	Per cent of infections starting on days indicated			
			5 or less	6-10 days	11-15 days	over 15 days
Total infections	163					
Serious	90	5*	54	6	5	5
Trivial	104	5*	60	37	0	3
No sulfonamide						
Total infections	40					
Serious	5		54	30	18	5
Trivial	5		36	36	3	
Sulfonamides						
Total infections						
Serious	44		40	40	5	5
Trivial	79		63	36	3	5

*Time of onset of infections not recorded

other groups although the differences are not statistically significant they all point in the same direction with one close exception in the smallest group this direction favors the controls.

It is possible that there are factors still operating within these groups to make the controls and the drug treated cases uncomparable such as the factor of severity. This warrants a further breakdown into groups containing two or more factors simultaneously. Such a cross tabulation furnishes data for Table IX in which two major factors are combined in a single group thus lessening the chance of heterogeneity. In this table also is found a consistency which is significant. In all but one line of figures (which represents the smallest group) the percentage of total infections for the drug treated cases is higher than that of the controls. In two others the serious infection rate in the controls is slightly higher than in the drug treated cases but this difference is offset by a lower rate in the trivial infections. In only two categories are the numbers large enough and the differences great enough to be statistically significant and are in favor of the controls but the general trend is also significant and is not in favor of the sulfonamides.

Table X illustrates a further breakdown into categories combining three of the major

TABLE XII.—SOFT PART WOUNDS INCIDENCE OF INFECTION IN CASES YIELDING THE MAIN GROUPS OF PATHOGENIC BACTERIA IN CULTURES OF THE DEBRIDED TISSUE

	Totals	Per cent infections			
		None	Serious	Trivial	Total
Hemolytic streptococcus Found in cultures	53	60	5	5	53
Not found in cultures	8	8	5	5	5
Total	26	5	6		17
Coccal positive Staphylococcus aureus Found in cultures		71	5	9	5
Not found in cultures	35	8	5	5	5
Total	26	8	6		17
Pathogenic aerobic gram negative bacilli Found in cultures			5	16	5
Not found in cultures	70	8		16	5
Total	26	8			17
Clostridium welchii Found in cultures		76		5	23
Not found in cultures	71	8	5	16	5
Total	26	8	4		17

5 statistically significant differences

factors concerned with wound infections but only those combinations are shown in which these three are either all maximal or all minimal. As the numbers in any one group decrease the variations become greater. In the three smallest groups the differences slightly favor the sulfonamides but these differences are not statistically significant. In the three largest groups the differences are significant and favor the controls but these are all in cases in which the major factors favoring wound infections are minimal.

From Tables VIII IX and X, therefore the figures seem to indicate that in those wounds in which the major factors which would favor wound infections are minimal these cases do better without the drugs. In the cases in which those factors are maximal the issue is not so clear but the weight of evidence is still not in favor of the sulfonamides.

The irrigation of wounds has been the subject of much discussion in the meetings of the committee. In the early part of the study it was the habit of some of the surgeons to have beside the operating table a stand to hold an irrigation can. Before debriding the wound

TABLE XIII—SOFT PART WOUNDS INCIDENCE OF HEMOLYTIC STREPTOCOCCI AND COAGULASE POSITIVE STAPHYLOCOCCUS AUREUS IN THE DÉBRIDED TISSUE THEIR PERSISTENCE IN LATER CULTURES AND THEIR LATER APPEARANCE IN CASES IN WHICH THEY WERE NOT ORIGINALLY FOUND WITH PARTICULAR REFERENCE TO DRUG TREATMENT

	Hemolytic streptococcus			Coagulase positive Staphylococcus aureus		
	Débrided tissue	Per staining	New	Débrided tissue	Per staining	New
Total	35		8	7	0	5
Serious infection	0	4	6	7	3	14
Trivial infection	13	5	6	4		27
Controls Total	4		4	7		9
Serious infection			3			
Trivial infection						6
Sulfonamide cases: Total	41		14	57	5	4
Serious infection	9	4	3	5		
Trivial infection		5	3	3		

*This does not include other coagulase positive micrococci

TABLE XIV—SOFT PART WOUNDS INCIDENCE OF PATHOGENIC AEROBIC GRAM NEGATIVE BACILLI AND CLOSTRIDIUM WELCHII IN THE DÉBRIDED TISSUE THEIR PERSISTENCE IN LATER CULTURES AND THEIR LATER APPEARANCE IN CASES IN WHICH THEY WERE NOT ORIGINALLY FOUND WITH PARTICULAR REFERENCE TO DRUG TREATMENT

	Pathogenic aerobic gram-negative bacilli			Clostridium welchii		
	Débrided tissue	Per staining	New	Débrided tissue	Per staining	New
Total	47	26	23	38		9
Serious infection			8	3	4	3
Trivial infection	30	8	9	9	3	4
Controls Total	44	7	7	37		
Serious infection	4	3				
Trivial infection	3		5	7		
Sulfonamide cases Total	3	0	26	06		7
Serious infection	7	8	6		4	
Trivial infection	7	7	14			2

infection in the accidental soft part wounds which have been covered in this study.

The question has been asked whether the use of the sulfonamides will delay the onset of infection. It is of interest to note the day of the development of infection and correlate it with the method of drug therapy (see Table VI). When division is made into 5 day periods it is seen that the largest proportion of the serious infections developed in the first 5 days while the largest percentage of the trivial infections developed in the second 5 days. It is seen that this was true both with the controls and with the patients treated with drugs. The figures for the first 5 days for both serious and trivial infections among the drug treated patients are slightly lower than in the controls suggesting that there was a slight delay in the onset of infection but the differences are not statistically significant because the series are small.

Of primary importance are of course the kind and degree of bacterial contamination. An attempt was made in one unit to make a quantitative determination of the number of organisms present but this was not found

it would frequently be subjected to extensive irrigation and in many cases this went on all during the operation. When the results of prolonged irrigation began to appear in the reports this method was largely abandoned and the dry débridement, often with two sets of instruments took its place. This is the more rational procedure for by it the great majority of the contaminating organisms are removed before there has been an opportunity to spread them around the wound. After débridement an irrigation of all loose particles which can be done in a few minutes may be of value. These cases have fallen into the short irrigation time group and cross tabulations seem to indicate that this factor *per se* is of some importance.

Many more similar cross tabulations have been made but they only confirm the results in the ones presented above which seem to illustrate the point clearly. No matter how we look at these results we cannot find any evidence to support the idea that the use of the sulfonamides has lowered the incidence of

TABLE XV—SOFT PART WOUNDS CROSS TABULATIONS BETWEEN BACTERIOLOGY AND COMPLETE CLOSURE OF WOUND WITH PARTICULAR REFERENCE TO DRUG TREATMENT

	Wound completely closed					
	Hemolytic streptococcus			Coagulase positive staphylococcus aureus*		
	Debrided tissue	Per meeting	New	Debrided tissue	Per meeting	New
Total	46	7		58		36
Serious infection	7		5	5		
Trivial infection					8	
Controls Total	12			5		
Serious infection			3			
Trivial infection						6
Self-made cases Total	33		8	43		27
Serious infection						8
Trivial infection		4	4	8	8	5

*This does not include other coagulase positive micrococci

feasible. It cannot be claimed that all of the qualitative analyses of the bacterial flora were complete or that the rarer species of organisms were always properly classified but the positive findings of the four main groups of pathogens seem reasonably accurate.

Table VII shows the frequency with which the four main groups of pathogens were found in the debrided tissue. It is seen at once that when these were found the incidence of infection ran higher than when the organisms were absent.

Tables XIII and XIV show not only the occurrence of these bacteria in the debrided tissue but also the number of times these four groups of organisms persisted and in how many cases these organisms were found later when they were not found originally suggesting either a secondary contamination or the persistence of organisms originally present in such small numbers that they were missed in the first culture. Furthermore the presence, persistence and new appearance of these organisms have all been correlated with drug treatment and the presence or absence of wound infection. It would appear from these tables that the organisms disappeared as readily from the wounds of the control cases as

TABLE XVI—SOFT PART WOUNDS CROSS TABULATIONS BETWEEN BACTERIOLOGY AND COMPLETE CLOSURE OF WOUND WITH PARTICULAR REFERENCE TO DRUG TREATMENT

	Wound completely closed					
	Pathogenic aerobic gram-negative bacilli			Clostridium welchii		
	Debrided tissue	Per meeting	New	Debrided tissue	Per meeting	New
Total		6		16	6	7
Serious infection	5	6	6			
Trivial infection	5	5	5	7		
Controls Total	40	6	7	29		
Serious infection	5					
Trivial infection			5			
Self-made cases Total			5	49	5	5
Serious infection				7		
Trivial infection		4	8	16		3

Note. Minor drug groups omitted

from those receiving primary drug and we have no indication whatsoever that the drugs primarily administered either locally or generally or combined were able to eliminate these organisms from these wounds. This is just as true of the hemolytic streptococcus and the *Clostridium welchii* which are ordinarily considered susceptible organisms as it is of the coagulase positive staphylococci and other micrococci and the pathogenic gram-negative aerobic bacilli which are more resistant.

In considering the tables showing the incidence of the different organisms during the course of treatment one is struck by three things. First, the small proportion of cases in which pathogenic organisms were found in the original cultures of the debrided tissue which later developed clinical infection. This is particularly striking with the *Clostridium welchii* which was found in 138 cases while infection developed in only 32 and in only 2 of these was there clinical gas gangrene. Second the rather small proportion of cases in which the organisms that were found originally persisted in later cultures, for example 1/5 with the hemolytic streptococcus 2/9 with the coagulase positive *Staphylococcus aureus*, 1/6 with the pathogenic gram negative bacilli

and 1/11 with the *Clostridium welchii*. These figures indicate not only the thoroughness of the removal of the organisms along with the débrided tissue but the ability of the body to take care of those organisms which were left behind. Third although these organisms in some cases persisted in later cultures or appeared later for the first time there was not always evidence of clinical infection. This clearly indicates that the criteria of infection were not based on the presence of pathogenic organisms in the cultures but upon the clinical manifestations of their presence.

When the bacteriology is cross tabulated with the closure of the wound (see Tables XV and XVI) it is evident that in the closed wounds pathogenic organisms were frequently found in later cultures even though they were not recovered from the débrided tissue. This suggests that they were there originally in too small numbers to be cultured and yet were able to gain a foothold in the tissues and grow out later. It is not likely for example that in many of the 12 closed cases in which the hemolytic streptococci appeared as new cultures, they entered the wound as secondary contaminants coming from the respiratory passages of attending doctors and nurses however prevalent that may be with regard to open wounds as suggested by Colbrook, Miles, Hare and others. Furthermore both the persistence of pathogenic organisms in wounds which were closed and their appearance as new cultures not found originally occurred just about as frequently in the cases primarily treated with drugs as in the controls. Further studies with regard to the bacteriology will be reported later.

With regard to the blood levels and dosages of the sulfonamide drugs some interesting points are brought out in Table XVII. There is a slight but not statistically significant higher incidence of infection when the blood level in the first 48 hours was below 7 milligrams per cent than when it was above that figure. A little wider difference is shown in the figures for average blood levels during the next 8 days but this difference is almost entirely among the trivial infections. With doses of 9 grams or less in the first 48 hours the figures are again slightly but not significantly

TABLE XVII — SOFT PART WOUNDS DRUG DOSAGES AND BLOOD LEVELS WITH PARTICULAR REFERENCE TO THE INCIDENCE OF INFECTION

	Totals	Per cent infection		
		Serious	Trivial	Total
Free sulfa drug in sera blood levels (primary sulfonamide only)				
48 hour level				
Less than 7 gms	357*	9	43	33
7 gms or more	76*	6	5	87
Next 8 day level				
Less than 7 gms	385*	7	69	39
7 gms or more	36*	88	8	60
Systemic sulfonamide (primary sulfonamide only)				
In first 48 hours 1 drug therapy				
Less than 9 gms	30	9	48	4
9 gms or more	39	60	5	0
In 3rd through 6th days of drug therapy				
Less than 20 gms	30	6	4	30
20 gms or more	38	89	14	0

*These data not recorded on some of the summary sheets.

higher than when the dose was above that figure while the results during the next 8 days for those receiving less than 20 grams were actually a trifle lower than for those receiving more than that amount. In 508 cases of drug treated patients recording these data, there were 66 or 13 per cent which had some unfavorable renal reactions to the drugs and 35 or 6.9 per cent which had some other kind of reaction such as rash, fever or fall in red or white blood cells.

In spite of these far from satisfactory results with the sulfonamides in the prevention of infection in these accidental wounds there have only been 4 deaths from infection in all of these 926 cases. What does this signify? Perhaps the most plausible explanation is that the sulfonamides while they have not been able to prevent or minimize local infections have been able to prevent the general spread of infection to the rest of the body. Of these 4 fatal cases 3 were among the drug treated patients and one was among the controls but the drug treated patients all had serious injuries which may have contributed to the fatal outcome. When infection developed among the controls the worst cases were

TABLE XVIII.—SOFT PART WOUNDS SUMMARY OF 4 CASES, ALL WOUNDS CLOSED IN WHICH DEATH FOLLOWED INFECTION TOTAL CASE, 926

Case	Lesion	Operation	Primary drug	Secondary drug	Cause of death	Day of death	Principal organisms
Case	Avulsion of scalp	Debridement, closure with tension	None	Sulfadiazine	Meningitis	4th	Complete positive staphylococcus <i>Acidus proteus</i>
Case	Stab wound of chest, abdomen, diaphragm, and stomach	Debridement, closure without tension	Sulfanilamide locally, sulfadiazine generally	Sulfadiazine	Empyema	3rd	Hemolytic strept. Group F
Case	Gunsight wound of abdomen, perforation of ileum and caecum	Debridement, closure of perforations, closure of wound	Sulfanilamide in wound, sulfadiazine generally	Sulfadiazine	Peritonitis	3rd	<i>B. coli</i> , <i>C. welchii</i> , <i>Neisseria meningitidis</i>
Case 4	Gunsight wound of abdomen. Perforation of jejunum, rectum and bladder	Incomplete debridement, closure of perforations, partial closure with drainage	Sulfanilamide in wound, sulfadiazine generally	Sulfadiazine	Peritonitis and pneumonia	5th	<i>B. coli</i> , green streptococcus

treated with sulfonamide as was done with the fatal case so that we cannot say with certainty whether or not we would have had a higher incidence of sepsis and death among the controls if we had carried them through completely without drug (See Table XVIII.)

For this reason we will have to fall back upon all of our past experience in order to say that we consider this mortality from infection of 0.43 per cent extremely low for these serious accidental wounds of the soft parts.

We wish to make clear that the results of this study should in no way be interpreted to mean that the sulfonamides haven't an important place in the treatment of infection. However that rôle is not in the prevention of local infection in the wound but in the prevention of local infection from getting out of control by becoming general and causing sepsis and death. The problem of the development of local infection in these wounds still remains unsolved and it will not be solved until we can find some way for the sulfonamides or some other agent to be effective in wounds in the presence of damaged tissue.

COMPOUND FRACTURES

The problem of compound fractures is two-fold: one infection, the other bone healing and subsequent bone and joint function. Our records contain many valuable data on the latter phase of the problem, but in this report we have considered this problem only from the point of view of infection. The end result desired in compound fractures is a normally

functioning member with firm bony union and freely contracting muscle around the bone and freely moving joints on either end of the fractured bone. This end-result is materially altered or delayed by infection within or around the bone or by infection in the soft parts. Bone is less resistant to infection than are soft parts and it is frequently cut off from its blood supply either as a loose fragment or as the exposed end of the shaft which has been stripped of its periosteum. Infection may develop at once within the first few days after the injury or start up with the first efforts to obtain full motion of the part, or be dormant for months after the wound has apparently healed and suddenly or gradually develop after some trauma or some general lowering of resistance such as chilling or fatigue.

There were 674 compound fractures in this series with 14.1 per cent serious and 11.4 per cent trivial infections or a total of 25.5 per cent. Whereas there were twice as many trivial as serious soft part wound infections, the serious exceeded the trivial in compound fractures. This was to be expected because when bone becomes infected wound healing is usually delayed and hospitalization is usually prolonged. In many of the trivial cases only the soft parts were involved in the infection.

The compound fractures have been divided into major and minor. The former have included the large long bones of the upper and lower extremities in which the problem of bone overriding and angulation from muscle contraction and the necessity for either inter-

TABLE IX — BREAKDOWN OF THE CASES OF COMPOUND FRACTURES ACCORDING TO UNITS WITH PARTICULAR REGARD TO THE TYPE OF INJURY AND THE INCIDENCE OF INFECTION IN CASES OF DRUG TREATED PATIENTS AND IN CONTROLS

Hospital Units	Total cases	All for fractures			Minor fractures		
		Number of cases	Per cent infection		Number of cases	Per cent infection	
			Serious	Trivial		Serious	Trivial
Albion City	80	40	7.5	5	40	8	
Charity New Orleans	07	77	30.4	0.5	10	3.3	3.3
Chickadee General	8	45	3.3		17	5.4	5.4
Detroit Receiving	73	07	0.3	7.5	70	5	0.7
Johns Hopkins	58	4	5	5	8	00	0.7
Massachusetts General	4		27.3	0		4.5	0
Presbyterian, N. Y.	3	1	4.4	0.6	0	5	00
Totals	674	4.4	6.9	9.9	260	0.6	3.8

Hospital units	Total cases	Sulfonamide cases			Controls		
		Number of cases	Per cent infection		Number of cases	Per cent infection	
			Serious	Trivial		Serious	Trivial
Albion City	80	75	8.0	0.3	4	7	00
Charity New Orleans	07	04	3.7	7.7	3	33.3	33.3
Chickadee General	8	08	8	4		00	00
Detroit Receiving	73	70	9	7	07	3	0.6
Johns Hopkins	58	58	3	3.8		00	00
Massachusetts General	4	30	3	20.5	3	33.3	00
Presbyterian, N. Y.	3	67		9	50	5	7
Totals	674	487	4.8	0	87		8

nal or external fixation are of major importance. All of the others have been classified as minor. Table XIX divides the 674 compound fractures into major and minor according to their occurrence in the different hospital units and also divides them into drug treated cases and nondrug treated controls in each hospital unit, with the incidence of serious and trivial infection in all four groups. This table shows variations among the different units in the material available for study and in the methods of treatment variations which are inherent in the set up of the different groups and yet which tend to balance one another. For

TABLE XX — PERCENTAGE OF INFECTION IN COMPOUND FRACTURES OF THE DIFFERENT MAJOR LONG BONES

	Total cases	Per cent infection		
		Serious	Trivial	Total
Humerus	43	4.4	8.9	5.3
Radius	7	5.0	1.8	0.7
Ulna	8	7	3.6	7
Radius and ulna	4		7.5	7.5
Femur	30	3.3		33.3
Tibia	7	0.7	8.3	5
Fibula		0	00	0
Tibia and fibula	7	4	.8	30.8
Totals	414	6.0	9.9	26.8

example at Massachusetts General the minor fractures outnumbered the major 3 to 1 while at Presbyterian in New York there were 5 major to 1 minor and at Charity in New Orleans the latter proportion was 2 to 1. Among the minor fractures at Presbyterian all of the infections were serious while at Johns Hopkins they were all trivial but both groups were small. In the major fractures however all units found the serious outnumbering the trivial. When grouped together it is seen that in the majority of the major fractures infections were serious while among the minor fractures the reverse was true. Only four of the units used any appreciable number of controls and two of these only started to observe controls in the latter part of the study. In the whole group there were two and a half times as many drug treated cases as controls but neither of these two groups show any preponderance of those factors which favor infection. They therefore seem to be fairly comparable. This will be brought out clearer in the later tables. Table XX shows the incidence of infection for each of the major bones. It is seen that the total number of cases as well as the percentage of infection is much higher in the lower extremity than in the upper both bones of the leg being the most common lesion and giving the highest percentage of both serious and trivial infections with the femur coming a close second.

The principal factors concerned with the incidence of infection in compound fractures

TABLE XXVII.—COMPOUND FRACTURES COMPARING THE DRUG TREATED CASES WITH THE CONTROLS WITHIN SUBGROUPS COMBINING THREE OF THE MAJOR FACTORS CONCERNED WITH WOUND INFECTION

	Controls				Sulfonamide cases			
	Per cent infection			Total cases	Per cent infection			Total cases
	Severe	Trivial	Total		Severe	Trivial	Total	
Greater contamination and greater tissue damage and open or partly closed wound	5.38	13.6	7	3.3	0.4	3.6	3	4.9
Greater contamination and greater tissue damage and completely closed wound	4.8			30.8	13.8	3.4		3
Greater contamination and lesser tissue damage and open or partly closed wound	33.3	33.3	60.6	6	10.7	0.0		6.7
Greater contamination and lesser tissue damage and completely closed wound	4.0	0.0	4.0	3.8		5	3.6	
Lesser contamination and greater tissue damage and open or partly closed wound		5	10	3.4	1.3	8	17.8	
Lesser contamination and greater tissue damage and completely closed wound		5	20	3.4	3	7		
Lesser contamination and lesser tissue damage and open or partly closed wound	0.0			3	0.0			
Lesser contamination and lesser tissue damage and completely closed wound	1.8	5.6	7.6	1.0	8	3		

8 Statistically significant differences

TABLE XXVIII.—COMPOUND FRACTURES DAY OF ONSET OF SERIOUS AND TRIVIAL INFECTIONS CORRELATED WITH THE CASES RECEIVING DRUG TREATMENT AND WITH THE CONTROLS

	Number of cases	Not controlled	Controlled	Per cent of infections starting on days indicated			
				5 or less	6-10 days	11-15 days	over 15 days
Total infections							
Serious	5	0*	26			13	25
Trivial		5*	6	8	16		48
Controls							
Total infections	7						
Serious	4.3				7	17	37
Trivial	2.4	0*	3.4	5	50		8
Sulfonamide cases							
Total infections	5						
Serious	7	8*	6.4	3		23	34
Trivial	2.3	5*	3.6	10	3	48	

*Data regarding time of onset of infection are missing in these cases

TABLE XXIX.—COMPOUND FRACTURES INCIDENCE OF THE MAJOR PATHOGENIC ORGANISMS CULTURED FROM THE DEBRIDED TISSUE AND THE PER CENT OF INFECTION IN THOSE CASES

	Totals	Per cent infection	
		Serious	Trivial
Hemolytic streptococcus Found in cultures	30	8.22	5.26
Not found in cultures	67	1.3	20.3
Coccal positive staphylococcus aureus* Found in cultures	54	8	18.7
Not found in cultures	690	1.4	
Pathogenic aerobic gram negative bacilli Found in cultures		8.5	
Not found in cultures	603		11.7
Clostridium welchii Found in cultures	147	8.23	12.6
Not found in cultures	577	8	
Combined pathogenic organisms Hemolytic streptococcus and coccal positive staphylococcus aureus	8	5	37.5
Hemolytic streptococcus and clostridium welchii	17	35	39.4
Coccal positive staphylococcus aureus and clostridium welchii	29	27.6	37.6

*This does not include other coccal positive micrococci

8 Statistically significant differences

When comparisons are made in Table XXVI between the controls and the drug treated

framework of the different factors which play a rôle in wound infection (Table XXV) we find only one statistically significant difference and that favors the controls. What is more significant is the fact that in those groups in which the factors which favor wound infection are maximal the figures for the drug treated cases in all but 1 instance exceed the figures for the controls. In those groups in which the factors which favor wound infection are minimal the controls are higher except in the category of small areas.

TABLE XXX—COMPOUND FRACTURES INCIDENCE OF HEMOLYTIC STREPTOCOCCI AND COAGULASE POSITIVE STAPHYLOCOCCUS AUREUS IN THE DÉBRIDED TISSUE THEIR PERSISTENCE IN LATER CULTURES AND THEIR LATER APPEARANCE IN CASES IN WHICH THEY WERE NOT ORIGINALLY FOUND WITH PARTICULAR REFERENCE TO DRUG TREATMENT

	Hemolytic streptococcus			Coagulase possit staphylococcus aureus*		
	Dé-brided tissue	Per sisting	New	Dé-brided tissue	Per sisting	New
Total	50	3	1	54	9	1
Serious infection		3	0	8	7	
Trivial infection	3		8	0	7	
Controls Total	7	3				7
Serious infection	3		7		1	
Trivial infection	5		3			
Sulfonamide cases Total		9	20	4	3	45
Serious infection	8	5	0	5	4	17
Trivial infection	7		4	8	0	

*Does not include other coagulase possit mikroococci
Minor drug groups omitted.

TABLE XXXI—COMPOUND FRACTURES INCIDENCE OF PATHOGENIC AEROBIC GRAM NEGATIVE BACILLI AND CLOSTRIDIUM WELCHII IN THE DÉBRIDED TISSUE THEIR PERSISTENCE IN LATER CULTURES AND THEIR LATER APPEARANCE IN CASES IN WHICH THEY WERE NOT ORIGINALLY FOUND WITH PARTICULAR REFERENCE TO DRUG TREATMENT

	Pathogenic aerobic gram negative bacilli			Clostridium welchii		
	Dé-brided tissue	Per sisting	New	Dé-brided tissue	Per sisting	New
Total		20	35	7		4
Serious infection	8	1	7	38		5
Trivial infection		4	1	7		
Controls Total	20	6		47	64	3
Serious infection	3		5	5	5	
Trivial infection	4	3		3		3
Sulfonamide cases Total	78		28	9	3	8
Serious infection	3			20	7	4
Trivial infection	6		6			

Note: Minor drug groups omitted.

cases by cross tabulations which combine two major factors concerned with wound infection the numbers in each group become smaller and variations increase in number but it is to be noted that in the two categories in which those factors are maximal the figures for the drug treated cases are higher than the control figures although the differences fall just short of statistical significance.

Table XXVII shows a further breakdown of the figures to combine three major factors. This table finds still more variations in the figures but the only significant difference is in the category in which all three factors are maximal and this difference favors the controls.

From these three tables XXV, XXVI and XXVII the evidence seems to be clear that in those situations in which local wound infection is favored to develop the sulfonamides as they have been used in these civilian compound fractures under study have failed to demonstrate any definite prophylactic value.

It is of interest to note the difference in the time of the development of the infection in

compound fractures as compared with soft part wounds and to correlate this time factor with the use of drugs. This is shown in Table XXVIII. It is seen that the onset of infection is frequently late a large percentage of both serious and trivial infection appearing for the first time after 15 days. The question has been asked whether the sulfonamides delay the development of infection in these wounds or render them less serious but this table gives no evidence to that effect. In the patients receiving drug treatment we find no lowering of serious infections as compared with the controls and if anything an earlier development.

Of major importance in the development of infection in compound fractures is of course the presence of pathogenic bacteria. Cultures of all of the débrided tissue reveal many species, and it will require special study to determine the significance of all of the organisms found. The tables shown herewith are concerned only with the four major pathogenic groups of organisms. Table XXX gives the incidence of the hemolytic streptococci the

TABLE XXXII—COMPOUND FRACTURES DEATHS FROM INFECTION—CASES IN A TOTAL OF 67

Case	Bones	Operation	Primary drug	Date of death	Principal organisms
Case	Tibia, fibula, ulna	Partial closure without tension. Plaster	Local sulfanilamide General sulfadiazine	oth	Case pos. <i>Staphylococcus aureus</i> , green streptococci, <i>C. thermophilus</i>
Case	Forearm, tibia and fibula	Partial closure with tension. Plaster	Local sulfanilamide General sulfadiazine	oth	Case pos. <i>Staphylococcus aureus</i> , <i>E. coli</i> , <i>S. proteus</i> , <i>S. pyocyaneus</i> , <i>C. sporogenes</i>

coagulase positive *Staphylococcus aureus*, the pathogenic gram negative aerobic bacilli, and the *Clostridium welchii* in the débrided tissue. The per cent of infection in the cases in which these were found is contrasted with the per cent of infection in the cases in which they were not found. It is seen that in all of these four groups the incidence of infection is higher where they were found. Except with the *Staphylococcus aureus* these differences are significant. This number would have been considerably augmented if other coagulase positive micrococci had been added. Combinations of these pathogens give a still higher incidence of infection but the number of cases in these categories is small.

Of greater interest still are Tables XXX and XXXI which show the number of cases in which the organisms, originally found in the débrided tissue persisted in later cultures and the number of cases in which they appeared as new cultures not originally found. All of these data are correlated with the method of treatment in the three major categories of sulfonamide therapy and in the controls. In these tables it is seen that the wounds were generally more highly contaminated with pathogenic organisms than were the soft part wounds and a higher proportion persisted than in the wounds of the soft parts. A little over $\frac{1}{4}$ of the hemolytic streptococci a little over $\frac{1}{3}$ of the coagulase positive *Staphylococcus aureus* strains $\frac{1}{6}$ of the pathogenic aerobic gram-negative bacilli and $\frac{1}{7}$ of the *Clostridium welchii* persisted. Thus it is evident that the débridement of the wound and the defense of the body rid the wound of the great majority of the contaminating organisms, but this holds true no more for the sulfonamide treated patients than for the controls. Furthermore the use of the sulfonamides did not prevent pathogenic organisms from appearing anew when

they were not found in the débrided tissue arising either from organisms present in such small numbers that they were not originally found or from organisms gaining a foothold as secondary contaminants. This holds true of the wounds which were closed as well as of those which were left open.

In spite of the unsatisfactory record of the sulfonamides as preventatives against local infection in these compound fractures, only 2 deaths from infection occurred (0.3 per cent) in the whole series. In both of the fatal cases the patients suffered injuries which were severe and played a part in the fatal outcome. Brief summaries of these cases are shown in Table XXXII. It is seen that both of these patients had local and general sulfonamide treatment and although they died they did not have septicemia. When infection developed in the control cases sulfadiazine was generally administered and in these cases there were no deaths and none with septicemia. It seems fair to conclude therefore that while the sulfonamides failed to prevent local infection in compound fractures they have minimized the general spread of the local infection and may have reduced the number of deaths. But the problem of the prevention of local infection remains unsolved and will have to await the discovery of some new form of sulfonamide or some entirely new agent which will be bacteriostatic or bacteriocidal in the presence of damaged tissue.

BURNS

The problem of severe burns has five phases—shock, toxemia and nitrogen imbalance, infection, slough separation and repair. While these five phases reach peaks of importance at different periods during the course of illness, they overlap to some extent. Infection has always been a serious problem in burns. Since the recent development of better understand-

ing and improved treatment for burn shock infection has become of greater importance because of the large number of seriously burned individuals that have survived the shock phase. Infection is of importance prophylactically from the moment of injury until the whole area is again covered with skin. Burns differ from other wounds in two important respects: first, they are usually extensive but not deep while other wounds are relatively deep but not extensive; second, it is not often possible or advisable to remove the dead tissue at the first surgical procedure as it is with other wounds. These two facts are important from the point of view of infection because the contamination with organisms is greater and impossible to remove and the medium which sustains their growth that is dead tissue remains to favor their development. The bacteria causing infection in burns may be those residing normally in the hair follicles or sweat glands or those deposited on the surface subsequent to the burn. A superficial burn caused by low temperature applied for only a short duration may not kill all of the organisms in the hair follicles. A deep burn caused by a higher temperature applied for a longer time probably kills all of the bacteria in the skin in the central areas but at the margin there must always be areas where the burn becomes superficial and the organisms which are there remain viable and capable of growth. In every case of burn there are three zones: one in which the tissue is killed directly by the heat; one in which it is injured but not immediately killed; and the third in which it is not injured at all. The thickness of these zones depends on the degree of heat and the duration of its application and the location on the body. Some of the injured tissue later dies and some recovers. A separation of the slough takes place between the living and the dead and the time of its separation depends on a number of factors of which infection is one.

In this study the clinical observers have tried to maintain a uniform conception of the meaning of the terms second or third degree burns and serious and trivial infections. In this study a second degree burn means one in which the superficial epithelium is injured to the extent of blistering and any

thing more severe than that short of a complete destruction of the deepest epithelial elements so that restoration can take place from residual epithelium. A third degree burn has all of the epithelial elements destroyed so that epithelial repair has to take place from the margin or from skin grafts. It is obvious that the degree of any burn cannot be determined when the patient arrives at the hospital or indeed until the repair has taken place or has failed to take place spontaneously. Furthermore, there cannot be a sharp line between a deep second degree burn where repair takes place from scattered residual islands of epithelium and a superficial third degree burn. In this study burns that have had any amount of third degree areas have been placed in this category and an attempt has been made to estimate as nearly as possible the per cent of the body so involved. Similarly in those which have only second degree areas the per cent of body surface has been approximately determined according to the scheme of Berkow.

With extensive surfaces involved it is obvious that cultures taken from the surface will invariably reveal many kinds of organisms both at the time of admission to the hospital and all during the course of the illness, but in this study burns have only been called infected when in the judgment of all of those caring for the patient there was clinical evidence of a reaction of the body to the presence of organisms or their products. A serious infection has been distinguished from a trivial infection when there was clinical evidence of a general as well as a local reaction of the body to the infection or further destruction of tissue by the infection or a materially prolonged hospitalization due to the infection. In some cases it is most difficult to decide whether or not infection has occurred or whether it should be called serious or trivial because there is often some reaction of the body, both local and general, to the presence of dead tissue during the course of its separation from the body.

When this study was initiated there was a great diversity of opinion with regard to the best forms of treatment. These could be grouped in three main categories: (1) tannic acid; (2) vaccine; (3) vaccine with empyreuma.

TABLE XXXIII—INCIDENCE OF INFECTION IN BURNS IN THE DIFFERENT HOSPITAL UNITS WITH SPECIAL REFERENCE TO THE DEGREE OF BURN AND SULFONAMIDE THERAPY

Hospital units	Total cases	Second degree		Third degree	
		Number of cases	Per cent infection	Number of cases	Per cent infection
		Second	Third	Second	Third
Akron City	5	43		8	
Charity New Orleans	65	8	66	18	
Cincinnati General	8		60	50	5
Cook County	5	10	10	1	9
Detroit Receiving	34	7	26.8		30
Henry Ford		30	6	3	39
Johns Hopkins		5	50	00	40
Massachusetts General	14*	8	57	76	
Presbyterian, N. Y.	66	7	8	54	
Totals	221	295	8	27	296

TABLE XXXIV—MAJOR FACTORS IN THE INCIDENCE OF INFECTION FOLLOWING BURNS

	Total	Per cent infection	Per cent infection
		Second	Third
Second and third degree	296	8.35.5	8.32
Second degree only	295	8.8	8.7
Greater gross contamination	206	8.27.8	27
Lesser gross contamination	5.5	8.16.9	11.8
Greater tissue damage	296	8.27	8.24.5
Lesser tissue damage	20	8.5	8.17
Operation after 3 hours	29	11	17.5
Operation before 3 hours		20.7	
Area over per cent body surface	69	8.5.5	26.6
Area less than per cent body surface	30	5.5	3
Shock	82*	5.26.5	71
No shock	401*	8.20.5	9

*Data missing in few cases.
 †Statistically significant differences.

Hospital units	Total cases	Sulfonamide cases		Controls	
		Number of cases	Per cent infection	Number of cases	Per cent infection
		Second	Third	Second	Third
Akron City	5	6	9	5	00
Charity New Orleans	65	3	38	20	26
Cincinnati General	8		26.8	5.8	3
Cook County	5	26	3.5	26	
Indiana Receiving	34	5	27.2	20	28
Henry Ford	63	3.6	26.8		26.8
Johns Hopkins		5.3	7		00
Massachusetts General	14*	54.5	0		20
Presbyterian, N. Y.	10	66	11.8	23	38
Totals	221	29	3.4	26	20.2

*This does not include the burns from the Corcoran Grove disaster. For each an opportunity was given for primary bacteriological study. Of the 26 burns of the skin, 10 did not die of pulmonary injury in the first days there were 14 serious infections and 12 infections.

dressing and (3) some form of sulfonamide. Even these did not satisfy all of the clinical observers and some desired to try out other frankly experimental methods. While it was recognized that if the number of categories were large the number of cases in each category would be small, it was felt that during the first year at least certain latitude should be given each unit to try out new methods

with the proviso that at least two methods be consistently compared with one another in order to have some controls. In most of the units some sulfonamide method was compared with a nonsulfonamide method. Beside the variation in the local form of treatment, the opportunity was offered to either administer or withhold general drug therapy. It was recognized that the hemoconcentration and the fall in blood pressure commonly occurring in severe burns, would increase the risk of toxic effects from kidney blockage with the sulfonamides. Therefore the general administration of the drugs was done cautiously particularly when large areas were covered by drug bearing local applications. All of the foregoing circumstances have diversified the methods of treatment in these cases, and yet it is believed that some order has been achieved out of chaos and some conclusions may properly be drawn from an assemblage and analysis of the data. Five hundred and ninety-one cases have been analyzed with serious infection observed in 21.8 per cent and trivial in 24.7 per cent or a total of 46.5 per cent infections.

Table XXXIII shows the breakdown according to hospital units with particular reference to the degree of the burn and the use of the sulfonamides. As with the soft part

TABLE XXXV — COMPARISON OF SULFONAMIDE TREATED CASES AND NONDRUG TREATED CONTROLS IN 2ND AND 3RD DEGREE BURNS

	Second degree				Third degree			
	Number of cases	Percentage infection			Number of cases	Percentage infection		
		Serious	Trivial	Total		Serious	Trivial	Total
N. sulfonamide	58	7.0	27	4	4	35	70.3	6.5
Sulfonamide	127	9.5	16.8	26.3	54	13	34	70
General without local sulfonamide	27	1	8.5	20.6	16	14.7	3.7	7
Local without general sulfonamide	27	5.4	6	27	14	8	47	5.9
Both general and local sulfonamide	73		3.7	4.7	64	50	26.6	76.6

wounds and the compound fractures this table reveals that there were differences between the units probably due not only to inherent differences in the available material for study but also due to variations in the interpretation of the definitions of second and third degree and serious and trivial infections mentioned above. For example it is seen that in the Akron and Henry Ford units the burns were predominantly second degree while at Chanty and Johns Hopkins they were predominantly third degree and in the other five units they were fairly equally divided. Furthermore the majority of the infections in the third degree burns were considered serious at Charity and Cincinnati and particularly at the Massachusetts General while all of the infections for third degree burns were considered trivial at Johns Hopkins. With regard to the distribution of drug treated and non drug treated cases we find that four of the units had more sulfonamide cases than cases without sulfonamide while in four the reverse is true and in one they are equally divided. This brings the totals approximately to equality. These differences or discrepancies do not invalidate the results for they tend to balance each other and they serve to emphasize the fact that in a study of this kind it is of the greatest importance to have it carried on in several different centers by several different groups of observers rather than to depend upon any one place to have available all types of cases or any one group of observers to make

TABLE XXXVI — BURN CASES RECEIVING LOCAL AND NOT GENERAL SULFONAMIDE WERE GENERALLY LESS EXTENSIVE THAN THE OTHER SULFONAMIDE GROUPS BUT THE DRUG TREATED CASES AS A WHOLE WERE SOMEWHAT MORE EXTENSIVE THAN THE CONTROLS

	Second degree		Third degree	
	Less than per cent body surface	per cent or more body surface	Less than per cent body surface	per cent or more body surface
N. sulfonamide	7	4		
Sulfonamide	27	40		3
General without local sulfonamide	4	3	45	
Local without general sulfonamide	3	5	30	4
Both general and local sulfonamide	2		47	7

completely accurate and unbiased observations.

Table XXXIV shows that the main factor in the incidence of infection in burns is the depth or degree of the burn. The cases are almost equally divided between purely second degree and those having some element of third degree but the former group had only 8.1 per cent serious and 17.0 per cent trivial infections while the latter had 35.5 per cent serious and 32.4 per cent trivial infections. Other major factors, as with soft part wounds and compound fractures, are gross contamination, tissue damage, surface area and shock. The factor of the time interval between injury and the first surgical treatments is not as important as it is in the other forms of injury studied. Approximately three quarters of the cases were treated within 3 hours.

When both the second and third degree groups are divided into those treated with some form of sulfonamide and those receiving no drug in any form we find that there is approximately the same number of treated and nondrug treated cases in each group. Table XXXV shows no evidence however that the use of drugs has lowered the incidence of wound infection. In this table the sulfonamide treated cases have been divided into three groups—general alone, local alone, and

TABLE XXXVII.—COMPARISON OF BURN DRUG TREATED CASES AND CONTROLS WITHIN THE SUBGROUPS WHICH INCLUDE THE MAJOR FACTORS CONCERNED WITH WOUND INFECTION

	300 case role				29 sulfonamide cases			
	Per cent infection			Total cases	Per cent infection			Total cases
	Total cases	Seri-ous	Triv-ial		Total cases	Seri-ous	Triv-ial	
Second degree only	58				4			5
Second and third degree	14	35	30	65	54			76
Greater contamination	6	5	9	45	10	26	36	60
Lower contamination		6	7	40				9
Greater tissue damage		9	26	54		26	36	54
Lower tissue damage	105				16			5
"Operation soon after	8		76	26				5
"Operation before	260	26			26	26		8
Shock	14	5	20	76				
No shock	276			20				24
Total burned area of body surface Less than 10 per cent					64	6		
10-20 per cent		6			16			
20-30 per cent	63	6			8	26		26
30-40 per cent or over	5	26			26			26
Total remaining area	176							

TABLE XXXVIII.—COMPARISON OF SULFONAMIDE TREATED BURN CASES AND NONDRUG TREATED CONTROLS IN THE SUBGROUPS OF THIRD DEGREE BURNS DIVIDED ACCORDING TO THE AREA INVOLVED WITHOUT REGARD TO THE EXTENT OF THE ASSOCIATED 2ND DEGREE AREAS

	Controls				Sulfonamide cases			
	Per cent infection			Total cases	Per cent infection			Total cases
	Total cases	Seri-ous	Triv-ial		Total cases	Seri-ous	Triv-ial	
3rd degree burn area of body surface Less than 5 per cent	80		14	52	86	3	36	67
5-9 per cent	26		8	23		36		26
10 per cent or over	76		26	2	26	6	9	66
Grafted cases Less than 5 per cent	20		26	15	5	40		25
5-9 per cent	26		23	5	8	25		25
10 per cent or over	1	7		1	27	9		1

S. S. statistically significant differences

drug treated cases in both the second degree (26% to 29%) and in the third degree (15% to 21%) groups but these differences are not statistically significant.

When the drug treated group and nondrug treated group are compared further within the subgroups pertaining to the major factors concerned with infection the results are of interest. They appear in Table XXXVII. In each of the categories the numbers are about equally divided except for shock. Shock *per se* may be a factor favoring infection but it has been thought that the factors producing shock are more important in that regard. In spite of this apparent weighting the sulfonamide group with more serious cases the per cent of infection in the shocked cases seems to be considerably lower thus apparently favoring sulfonamide treatment but the difference is short of statistical significance for the series is small. There seems to be also a preponderance of cases with greater contamination in the sulfonamide group but here the percentage of infection favors the controls and this difference is on the borderline of significance. In what is perhaps the most important category namely

combined—and each one has been studied for the incidence of infection in second and third degree burns. We find that with one exception all of the drug treated groups have a higher incidence of infection than do the nondrug treated groups. That exception is in the smallest group of third degree burns, namely that which received local without general sulfonamide. Here the per cent of serious infection is remarkably low. This low percentage is partly but not completely offset by a high per cent for trivial infections. When we look for an explanation of this apparent discrepancy we find that this group was largely composed of burns of small area, in both the second and third degree groups as is shown in Table XXXVI. This table also brings to light the fact that the controls had a lower percentage of extensive burns than the

TABLE XXXIX.—BY CROSS TABULATIONS A COMPARISON OF DRUG TREATED BURN CASES AND CONTROLS WITHIN THE SUBGROUPS COMBINING TWO OF THE MAJOR FACTORS CONCERNED WITH THE DEVELOPMENT OF INFECTION IN BURNS

	Controls				Sulfonamide cases			
	Per cent infection			Total cases	Per cent infection			Total cases
	Total cases	Seri-ous	Tri-vel		Seri-ous	Tri-vel	Total	
Greater contamination and greater tissue damage	95	30.5	26.4	56.9	4	20.6	14.7	6.1
Greater contamination and lesser tissue damage		4.8	4.8	9.6	26	5	5	31.4
Lesser contamination and greater tissue damage	97	26.8	5.5	5.6	74	24	22	4.6
Lesser contamination and lesser tissue damage	87	5.8	8	7.6	67	8		20.5
Greater contamination and no shock	5	46.7	3.9	70.6	1.3	3	6	
Greater contamination and no shock	99		2.3	44	1	20	20	5
Lesser contamination and no shock	9	55.5		77.7		3.6		5.6
Lesser contamination and no shock	7	4.6	4	25.6	20		20.8	35.8

"greater tissue damage" the numbers are almost equally divided both for the number of cases and for the percentage of infections.

The figures for area are of considerable interest. Here the total areas are given and in each group the figures for the drug treated cases are higher than for the controls. These differences would not of themselves be significant except that they all point in the same direction which is in favor of the controls. If we combine the factors of extent and depth in the third degree burns we find that in the smaller area burns the number of drug treated and non drug treated cases is almost identical both in the numbers of cases and the per cent of infections, while in the most extensive group there were more patients who received the drug and yet they had a lower percentage of infections. If however we count only those patients who lived long enough to have grafting done the difference is not so great and falls short of statistical significance. In all of these comparisons therefore we can find no clear cut

TABLE XL.—PERCENTAGE OF INFECTION ASSOCIATED WITH DIFFERENT FORMS OF LOCAL TREATMENT IN THE NONDRUG TREATED BURN CASES

	Second degree				Third degree			
	Number of cases	Percent infection			Number of cases	Percent infection		
		Seri-ous	Tri-vel	Total		Seri-ous	Tri-vel	Total
Vaseline with pressure	70	4.3	4	5.7	47	7.7	4.5	70
Boric acid with pressure	9			2.3		00	00	00
Lanolin with pressure		00	27.3	27.3	50			60
Saline with pressure	5	6.7	80	6.7	23	37	7.3	24.4
2% peroxide with pressure		9.3	33	42.8	5	24.8	20.4	6.5
Tannic acid	7	3	8.6	42.9	9	44.4	55.6	00
Quinbrecho tannin	4	5	5	7.5	5	60	20	80
Micellaneous		4.8	3.8	28.6		26.4	27.3	65.7
Totals	58	7	7	4	4	35	20.3	65.5

evidence of the value of the sulfonamides in the prevention of infection in burns except possibly in the most seriously and extensively injured group. Let us turn therefore to a further breakdown of the figures. When two of the factors are combined as in Table XXXIX, there are no differences of statistical significance except for one small group which favors the controls. In other categories there is little to choose between the two groups.

Tables XL, XLI, XLII and XLIII give the results for the various forms of treatment. As has been stated, the local treatment in these cases has been quite diverse in an effort to discover some outstanding method that would minimize infections. Table XXXV indicates that about one half of the cases had no sulfonamide drug treatment of any kind, one half of the remainder received sulfonamide both locally and generally while the other half was divided almost equally between those receiving drug locally but not generally and those receiving it generally but not locally. Each of these groups has been broken down into various categories of local treatment and within these groups the second and third degree burns have been compared. With both the drug treated and nondrug treated cases two principles of dressing have been used: one the com-

TABLE XLI — PERCENTAGE OF INFECTION ASSOCIATED WITH DIFFERENT FORMS OF LOCAL TREATMENT IN THE BURN CASES RECEIVING SYSTEMIC BUT NO LOCAL SULFONAMIDE

	Second degree				Third degree			
	Number of cases	Percent infection			Number of cases	Percent infection		
		Severe	Trivial	Total		Severe	Trivial	Total
Vaseline pressure	7		5		20			20
Boric acid with pressure	60	60	00				6	3
Lanolin pressure	66	60	00		8	5		
Vaseline with pressure	00	00	00	00	13	44	77	
Zinc peroxide with pressure	60				20	20	60	
Tannic acid	5	20	60		60	00	00	
Micoflaccous	08				20	20	80	
Totals		5	70	50	2	7		

TABLE XLII — PERCENTAGE OF INFECTION ASSOCIATED WITH DIFFERENT FORMS OF LOCAL TREATMENT IN THE BURN CASES RECEIVING LOCAL BUT NO SYSTEMIC SULFONAMIDE

	Second degree				Third degree			
	Number of cases	Percent infection			Number of cases	Percent infection		
		Severe	Trivial	Total		Severe	Trivial	Total
Sulfadiazine ointment		00	20	20.8	60	60.7	66.7	
Sulfadiazine spray		60	00	00		44	23.5	
Sulfathiazole ointment		00	60	60		60	00	60
Sulfonamide film	3	60	00	00	5	60	20	20
Sulfonamide powder		60	00	60		58	5	
Tannic acid and sulfonamide		60	60	00		60		
Micoflaccous	6	22	20	58		60	60	60
Totals	2	24	6	7	24	28.8	4	19

pression dressing over a powder or over a non-adherent ointment and the other an eschar forming preparation either tanning the skin or covering it with an adherent film and leaving it exposed. In some cases a preformed film was used together with a compression dressing.

In Table XL the nondrug treated cases are shown. The large number of categories has reduced the figures for each form of treatment

TABLE XLIII — PERCENTAGE OF INFECTION ASSOCIATED WITH DIFFERENT FORMS OF LOCAL TREATMENT IN THE BURN CASES RECEIVING BOTH LOCAL AND GENERAL SULFONAMIDE

	Second degree				Third degree			
	Number of cases	Percent infection			Number of cases	Percent infection		
		Severe	Trivial	Total		Severe	Trivial	Total
Sulfadiazine ointment		00				5	20	25
Sulfadiazine spray		60	20	20	8	20	60	80
Sulfathiazole ointment	8	60		5	27.3	5.5	7.3	
Sulfonamide film	5	40	40	80		20	60	80
Sulfonamide powder	35	00			100	60	100	
Tannic acid and sulfonamide		60			63.7	27.3	90	
Micoflaccous		00	60	60		35	5	40
Totals	3		2	4	3	20.6	26.6	47.6

with wide variations in percentages for infection. However a few general statements seem warranted. It is clear that there was a higher incidence of infection in third degree than in second degree burns for almost all forms of treatment. The chief consideration should be given to the third degree column. It is evident that the tannic acid cases did badly. This was so apparent in all of the units in the earlier reports that the method was discarded fairly early in the course of the study. For that reason the number of cases was small for both forms of tannic acid. Early favorable observations with boric acid ointment recommended it to the staff of the Massachusetts General Hospital when the Coconut Grove disaster came upon them. The facilities of the laboratory were swamped and it was not possible for them to make any primary bacteriological cultures. They have therefore not been included in this final summary. Six of the 39 cases had no surface burns. 6 died on the second to fourth day from inhalation burns, 1 was transferred on the second day. We have however the records of 26 of these cases and know that the per cent of infections was 54 per cent serious and 3.8 per cent trivial. Among the other methods of local treatment none is outstanding and the percentage differences are not significant.

TABLE XLIV — TIME OF ONSET OF THE INFECTION AS CORRELATED WITH THE USE OR NONUSE OF SULFONAMIDE TREATMENT IN 23 OF THE 275 CASES OF INFECTION FOLLOWING BURNS

	Number of cases	Not counted	Counted	Percent of infections occurring in each 5 day period			
				1-5 days or less	6-10 days	11-15 days	more than 15 days
Total infections	275						
Serious	20	2*	07	5	30.1	5.0	0
Trivial	46		5	9.8	8		
Control.							
Total infections	3						
Serious	6	5	36	3		4.0	5
Trivial	70	0	6	27.0	27.9	10	8
Sulfonamide cases							
Total infections	244						
Serious	68	7*	5	7.5	3	3.5	7.6
Trivial	76	2*	64	20.7	20.7	20.0	4

Data regarding time of onset of infection re missing these cases

Table XLI shows the same types of local treatment as in Table XL combined with the systemic administration of sulfonamide — usually sulfadiazine. These figures do not materially differ from those without the drug but in all but one category they are higher rather than lower for the third degree burns.

In Table XLII the cases are grouped according to the different local sulfonamide treatments none of these having received systemic sulfonamide. Table XLIII includes those cases which had both systemic and local sulfonamide. The figures for the combined treatment are no better than in those patients which received no general drug. No one form of treatment is outstandingly good. The tannic acid combinations and the powdered sulfonamide cases may be said to be inferior the latter group showing a particularly high percentage of serious infections. The sulfonamide film cases yield the lowest figures for the third degree burns, but the figure is high in the second degree group and the total numbers are small. Further observations with this form of treatment are needed.

From these four tables no one method of local treatment stands out above the others

TABLE XLV — INCIDENCE OF CERTAIN OF THE PATHOGENIC BACTERIA IN THE DEBRIDED TISSUE IN BURNS THEIR PERSISTENCE IN THESE CASES AND THEIR APPEARANCE IN OTHER CASES IN WHICH THEY WERE NOT ORIGINALLY FOUND WITH PARTICULAR REFERENCE TO SULFONAMIDE TREATMENT AND THE DEGREE OF THE BURN

	Second degree			Third degree		
	Debrided tissue	Persisting	New	Debrided tissue	Persisting	New
<i>Staphylococcus aureus</i> N. sulfonamide	5	3	6	16	5	5
Sulfonamide			3	5	7	
<i>Corynebacterium diphtheriae</i> N. sulfonamide			8		3	16
Sulfonamide	7	0		20		16
<i>Pseudomonas aeruginosa</i> N. sulfonamide	1	5		33	11	45
Sulfonamide	33	4		5		4
<i>Chromobacterium violaceum</i> N. sulfonamide	40	6		40	5	
Sulfonamide	40			40	5	

but taken as a whole the compression dressing method has been found to be superior to the eschar forming treatments.

The day of onset of infection is of interest as is shown in Table XLIV. The time of onset was not noted in some of the early cases but we have data of this kind for 232 of the 275 cases which developed infection. These have been divided into those receiving sulfonamide and those without sulfonamide and each of these main groups has been subdivided into 5 day units. It is seen from this table that in the whole series the peak of the serious cases developed in the second 5 day period while in the trivial cases the onset was fairly evenly distributed through the first 15 days. There is no indication from the figures on the table that infection in the sulfonamide treated patients was delayed by this treatment or that the infection was less serious than in the nondrug treated cases.

The bacteriology of burns covers a wide range if a careful analysis is made of the bacterial flora present in the loose skin removed from the burned area. Swab cultures are

TABLE XLVI.—DEATHS FROM INFECTIONS, 3 CASES IN A TOTAL OF 591 CASES

Cases	Degree	Region	Per cent of body surface	Local treatment	Primary general drug	Secondary general drug	Day of death	Principal organisms
Case 1	red and 3rd degree	Face, trunk, both arms and hands, right leg	66-70	Equal parts powdered sulfanilamide and sulfadiazine	Sulfadiazine	Sulfadiazine	5th	Coag. pos. staph. and hemolytic strept. group I, <i>S. pyocyanus</i> , <i>S. proteus</i>
Case 2	red and 3rd	Face, trunk and all limbs	66-70	Fibrinogen, thrombin, sulfadiazine	Sulfadiazine	Sulfadiazine	25th	Coag. pos. staph. hemolytic strept. group II, <i>S. pyocyanus</i> , <i>S. coli</i>
Case 3	red and 3rd	Face, trunk, upper extremities and thighs	40-50	Tannic acid before admission; vaseline with pressure after admission	None	Penicillin	24th	Coag. pos. staph. (septicemia) hemolytic strept. group I, <i>S. pyocyanus</i>

entirely inadequate and even the cultures of all of the tissue removed cannot reveal with certainty all of the organisms present in any given case. It will take some time to analyze the data especially with regard to the results with combination of organisms. For this report interest has been centered around the well known pathogenic organisms namely the hemolytic streptococcus the coagulase positive staphylococci the gram negative bacilli of the escherichia aerobacter typhoid-dysentery pyocyanus and proteus groups, the Clostridium welchii the anaerobic streptococci and other pathogenic anaerobes.

We have been particularly interested not only in the incidence of these organisms in the débrided tissue but the persistence of these organisms in the cases during the course of treatment and their later appearance as apparently new cultures in cases in which they were not originally found. These figures which appear in Table XLV are broken down to show the influence of the sulfonamides on this persistence and new development.

One is struck by the large number of cases in which these organisms are originally found which failed to develop infection and also by the comparatively large number of cases in which they appeared as new cultures. It is equally obvious from these charts that the primary use of sulfonamides has not been associated with the more thorough elimination of these organisms than in the control cases nor have they prevented the establishment of the organisms in the wound.

During the first year it was particularly evident that the anaerobes were more easily eliminated from these burns than were the

aerobes. Apparently the surface of dead skin does not offer the same favorable environment for growth and invasion as the muscular layers. It was therefore decided at the end of the first year to omit the anaerobic cultures on burns unless infection developed. No anaerobic cultures were taken in 204 of these burns. The incidence of anaerobes in the débrided tissue is therefore based on 287 cases, anaerobes being found in 261.

In spite of the apparently questionable value of the sulfonamides in the prevention of local infection in burns there were only 3 deaths from infection in the whole series—0.5 per cent. Brief abstracts of these cases are shown in Table XLVI. These were all second and third degree burns with 50 per cent or more of the body surface involved. Two were primarily treated with general sulfadiazine and one of these with local sulfonamide as well neither developed septicemia. The third had no general drug. Tannic acid had been used before admission but after admission the local treatment was changed to vaseline gauze and compression. Staphylococcus aureus septicemia developed in the 5th day and failed to respond to penicillin although death did not occur until the 24th day. This may be considered a low mortality from infection in burns. When the controls became seriously infected sulfonamides were often used systemically and we therefore have no control series carried through the whole course of treatment to compare with the mortality figures with the sulfonamide treated patients.

The sulfonamides have apparently been useful in treating cases of infection by reducing its spread from the original site. This has ap-

parently been done successfully in cases that were not originally treated with the drug. There is no indication from this study that these drugs should be used as prophylactic agents in cases of burns.

GENERAL SUMMARY

A study and an appraisal have been made of the use of sulfonamides as preventatives against wound infection in civilian accidental wounds of the soft parts, compound fractures and burns in order that there might be a rational basis established for their use in the prevention of infection in war wounds.

For this purpose nine units studied clinical cases in various parts of the country. A uniform method of gathering data has been used in an effort to record in every case the presence or absence of factors which might play a rôle in favoring or minimizing wound infection in the individual case. All of the cases have had the best possible surgical care of which the individual units have been capable. This has generally consisted in prompt operation and the removal of all of the devitalized tissue except in burns. Bacteriological studies have been made of the tissue removed from the wound and of material from the wound itself when indicated during the course of treatment—so that it might be known with what bacterial contamination the various forms of treatment had to deal and under what conditions each treatment succeeded in preventing infection and in what conditions it failed to do so.

The results in cases treated with sulfonamides have been compared with the results in nondrug treated controls. Although the number of controls in the different units has varied the importance of maintaining the controls as a strictly parallel series has been constantly kept in mind. One can be certain that there was no conscious selection of cases which might prejudice the results either in the controls or in drug treated cases. All of the responsible investigators and the clinical directors of the different units are agreed that the controls reported here offer a fair basis for comparison. Furthermore an analysis of the factors present both in the drug treated cases and in the controls seems to indicate that this true within the limits of control discussed

The data from 2 191 cases have been studied and analyzed with the aid of Dr. John Fertig, professor of biostatistics of Columbia University. Of these there were 926 soft part wounds, 674 compound fractures, and 591 burns.

The chief factors concerned with the development of infection in compound fractures and soft part wounds have been found to be (1) the degree and extent of tissue damage, (2) the degree of gross contamination by dirt and other foreign bodies, (3) the duration of time between the injury and the surgical care, (4) the nature of the bacterial flora in the wound and (5) the care and thoroughness with which the devitalized tissues, foreign bodies and gross contamination are removed from the wound. In burns the first four of these apply but the most important factor is the extent of the deep burn.

The use of the sulfonamides as employed in these cases either systemically alone or locally alone or combined has not materially reduced the incidence or the severity of local infections in the wounds or burns nor have they delayed the development of infection nor have they eliminated the pathogenic organisms from the wounds. It seems likely however that they have minimized the spread of the local infection into the general circulation and have therefore cut down the incidence of septicemia and death. This has been accomplished by systemic drug therapy when infection developed in the controls as readily as when the drugs have been used either locally or generally as prophylactic agents and employing them only as therapeutic agents after infection has developed. Omitting the routine early use of these drugs would avoid a great waste of material and many toxic reactions. However if this is done in a rush of military hospital work the onset of infection might be overlooked and septicemia might be established before the drugs could be effectively administered.

It was hoped that it would be possible to demonstrate by statistical methods that the sulfonamides were capable of materially reducing the incidence of infection in wounds treated under the conditions to be found in a number of good civilian hospitals. In fact it

was not beyond the hope of certain individuals that they would be able to do this in spite of certain compromises with surgical principles such as incomplete removal of devitalized tissue and gross contamination—such as might be necessary under the stress of military conditions or when careless ward dressings are done without due regard to the possibilities of secondary wound contamination from the hands or from the nose and throats of the attendants. But such was not the case. Our carefully analyzed figures show that when the local conditions favored infection the controls on the whole did better than the drug treated cases. These are precisely the conditions in which it was hoped that the drugs might be of value. This tends to lend weight to the belief that the presence of devitalized or damaged tissue in some way inhibits the bacteriostatic action of the sulfonamides.

The problem of secondary contamination has not been thoroughly explored although data on some of the points involved are available on the summary sheets and will be included in the later bacteriological report. Most of the units took special precautions to avoid secondary contamination of the wounds as far as local conditions permitted. The development of hemolytic streptococcus infections in closed wounds when that organism was not found in the debrided tissue strongly suggests that many of the organisms which develop a wound infection are among the primary contaminants but present in such small numbers that they are not recovered from the primary cultures.¹

All of the results seem to indicate that the main dependence of the surgeon in the preven-

tion of infection both in civilian accidental wounds, and in the war wounds must be placed upon the well known principles of the surgical care of contaminated wounds,—namely the removal of the devitalized tissue and the contamination and the rapid restoration of the normal physiology of the part involved. The use of the sulfonamides can in no measure make up for this.

The results of this study have surprised many people and are presented with the keen disappointment of all of those who have worked on the problem for all hoped that something would be found which would prevent infections in these wounds. However the facts must be faced the problems which they present must be understood and an attempt must be made to solve them because in war wounds, local infection even if it does not result in death, causes prolonged hospitalization and either temporary or permanent disability or deformity frequently with loss of limb. Effort must be made in the following directions (1) to find out what interferes with the bacteriostatic action of sulfonamides in the wound or on the surface of a burn (2) to find some way to inactivate the inhibitors (3) to find some form of sulfonamide which will not be inhibited in the wound (4) to find some other agent which will eliminate the bacteria from the wound or nullify their action without injury to the wound itself.

Certain of the units are pursuing these problems with particular reference to the prophylactic value of the microcrystals of sulfathiazole and of penicillin. Further studies must be made on other promising agents, such as the proflavines, the oxyquinolines, the carboxymethoxylamines, other oxidizing agents and radiotherapy.

¹The Lancefield grouping of the hemolytic streptococci found in these cases will be the subject of a separate report.

THE ABSORPTION OF SULFONAMIDES FROM THE BURN SURFACE

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FOLLOWING the rather extensive local use of sulfanilamide to prevent infection in wounds, it was only natural that since infection is one of the chief problems in severe burns sulfanilamide should have been used locally in burns. Unfortunately the clinical demonstration by Hooker and Lam that this practice may be associated with extremely high blood levels of sulfanilamide due to the ready absorption of sulfanilamide powder from the burned surface has not deterred some persons from advocating sulfanilamide ointment for the treatment of burns, without specifying the degree of absorption to be expected or the type of ointment to be employed.

The study reported here has been concerned with an attempt to ascertain the influence of the ointment base on the relative absorption of sulfonamides from the burned surface in patients with severe burns. In commercial pharmaceutical practice ointment bases are essentially of two contrasting emulsion types namely (1) oil in water in which the water phase is external and (2) water in oil in which the water phase is internal. Since sulfanilamide is practically insoluble in oil (7 to 8 mgm. per 100 c.c.) but relatively soluble in water (1500 mgm. per 100 c.c.) (4) it will be immediately surmised that there is a marked preferential solution of sulfanilamide in the water phase of the emulsion. Thus great differences are likely to be found in the relative absorption of the drug from the burned surface depending on which phase water or oil is continuous with the absorbing burned surface. That such is actually the case in clinical practice will be demonstrated.

The sulfonamide ointments studied were of the following compositions

Oil in water emulsion—('water dispersible base')	
Mineral oil	17
White wax	7
Water	61
Emulsifying agents	5
Sulfanilamide	5
Sulfathiazole	5

From the Department of Surgery, Medical College of Virginia.

This study has been carried out under contract, recommended by the Committee on Research, between the Office of Scientific Research and Development and The Medical College of Virginia.

Water in oil emulsion—(oil base)

	Per cent
White wax	5
Petrolatum	47
Paraffin	10
Water	23
Emulsifying agents	5
Sulfanilamide	5
Sulfathiazole	5
MICV ¹ ointment	
Peanut oil	12
Lanolin	41
Rose water ointment	41
Sulfanilamide	6
(100 mesh powder)	

Medical College of Virginia

It will be noted that the percentages of sulfanilamide and sulfathiazole are the same in each ointment type. The formula for our own oil base ointment is shown because of the many requests we have had for this information. The only essential and important pharmaceutical differences in the two ointments employed in this study are that they are two distinctly different types of emulsion. We believe that the two types are characteristic of the average ointments supplied by pharmaceutical houses or hospital drug rooms.

CLINICAL OBSERVATIONS

All burned patients were treated in essentially the same manner. There were 15 burn patients on whom the oil in water (water dispersible base) emulsion was used and 12 on whom the water in-oil (oil base) emulsion was used.

The same regimen of burn therapy was employed in each group. The burned areas were gently cleaned with soap and water, the easily removed skin excised, the ointment spread thickly over the burned area, and occlusive pressure dressings applied. Plasma and fluids were given as the patient's needs were indicated in each case by hematocrit studies every 6 hours. A blood sulfanilamide was determined on each hematocrit sample by the Marshall colorimetric method (No attempt was made to differentiate between blood sulfanilamide and sulfathiazole).

4. *Water dispersible base.* Four representative patients protocols and sulfonamide absorption charts are shown.

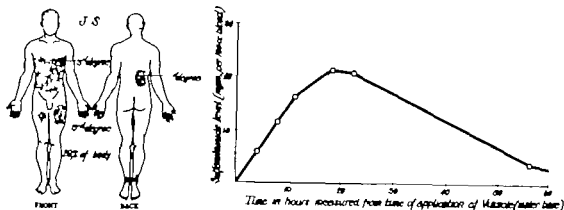


Chart 4. Extent of burn and sulfanilamide level in Case 4.

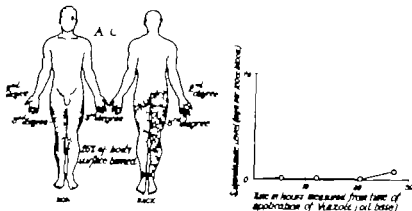


Chart 5. Extent of burn and sulfanilamid level in Case 5.

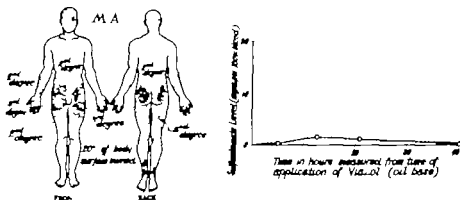


Chart 6. Extent of burn and sulfanilamid level in Case 6.

54%) and each 8 hours for days because hematocrit stayed around 54 to 58 per cent, until 7 hours. The face became tremendously swollen. Blood sulfonamide levels rose to 2.8 milligrams per cent. The face and shoulders healed without grafting, but grafting was needed on upper arms.

The case studies reported here indicate without any doubt that when sulfonamides are incorporated in an oily base very limited absorption of

the drug takes place. In contrast, when the water dispersible base is used, absorption is prompt and high blood levels of the drug may be reached. In a now extensive series of burns treated with an oily base ointment (Table I) in this hospital and reported earlier (2) we have been impressed with the limited absorption of sulfanilamide from the burned surface when our own oil base ointment is

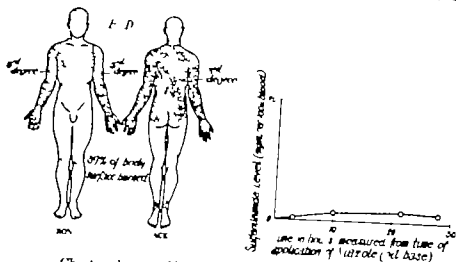


Chart 7 Extent of burn and sulfanilamide level in Case 7

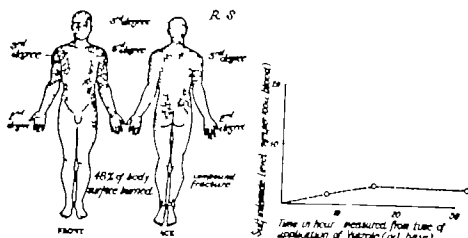


Chart 8 Extent of burn and sulfanilamide level in Case 8

used. We have yet to see any evidence of sulfanilamide toxicity when the oil base ointment has been employed in widespread burns (up to 75% body surface).

Observations reported recently by Gurd, Ackman, Gerne and Pritchard and Allen Owens, Evans and Dragstedt offer excellent supporting evidence that properly prepared sulfonamide ointments may be used with safety and indeed with the assurance that a low incidence of infection of surgical significance will result even if applied to large surface burns. Reference to these published works indicates that the Montreal group uses an ointment very similar to the oil base used in these studies while the Chicago group employs an ointment very similar to our own (MCV) ointment. With each of these oil base ointments, absorption of sulfonamides has been extremely limited.

We have been impressed by the cogent article of Lockwood who has defined with care the objectives to be desired in studies attempting to evaluate the benefits or dangers resulting from the local use of sulfonamides in wounds and burns.

We are aware that studies such as have been reported by the Montreal group (3) The University of Chicago group (1) and ourselves (even though the combined series now total something over four hundred burn cases and in which similarly prepared ointment and treatment philosophy have been used) do not settle with finality the arguments that have arisen of the wisdom of incorporating sulfonamides in burn ointments. Certainly in these series, the incidence of infection has been gratifyingly low.

We are aware of the report of Meleney that locally applied sulfonamides did not seem to reduce the incidence of serious infection in 347 cases of burns treated by a group of investigators in different localities. In that study sulfadiazine ointment, sulfadiazine spray (Pickerell) and sulfonamide powders were applied directly to the burned area. Presumably no oil base ointments, such as described in this report were studied.

We have continued to wash routinely and gently the burned surface with copious quantities of simple white soap and water and to excise care-

fully the easily removed skin before applying oil base sulfonamide ointments and pressure dressings. We are in firm agreement with Koch that such an attempt at surgical cleanliness is "simply common sense." What part this practice has played in materially reducing wound and burn infection in our hands is difficult to appraise. That it is significant is borne out by our recent experience in a small number of burns in which no sulfonamide was applied to the burned surface but the other aspects of our routine were adhered to. The incidence of burn infection was again very low. We shall continue this practice until it can be shown to our satisfaction that it is a useless step in burn therapy in the hospital. (Of course this step is not advocated in military surgery where conditions do not allow its proper application.) The significance of infrequent dressing of the burned areas is no wise less important, no matter what ointment is used.

SUMMARY

These studies indicate that the absorption of sulfonamides from the burn surface is limited when oil base ointments are employed. In con-

trast, when a water dispersible base is used toxic blood levels of the drug may occur. Results of studies on burned patients indicate that oil base sulfonamide ointments can be used with safety; their use has been attended with gratifying results of low incidence of infection.

If sulfonamides are to be incorporated in an ointment for use on burns, these studies indicate that an oil base should be used. Further studies on burn patients should be made to insure only limited, slow absorption of the drug before any such ointment is advocated for human use. In our experience an oil base composed largely of mixtures of lanolin and petrolatum has proved very satisfactory.

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CLOSURE OF DEFECTS OF THE SKULL WITH TANTALUM

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THE purpose of this paper is to stress the desirability of closing defects of the skull to point out the advantages of tantalum implants for this purpose, to illustrate the varying conditions under which they may be used to argue for screw fixation as compared with other means of fastening the implant, and to plead for the immediate repair of traumatic defects of the skull occurring on the field of battle.

NEED FOR CLOSING DEFECTS

The importance of closing defects in the skull whether they result from trauma or cranial operation, has not been sufficiently stressed. This is doubtless because the cranial defect is considered unavoidable and actually beneficial in providing decompression to relieve the accompanying intra cranial pressure. The obvious benefits in such cases have often blinded the surgeon to the deleterious effects of cranial defects in general. In the trephined patient the relation between the cranial defect and symptoms of dizziness, faintness, head pains, poor memory, irritability or convulsions is frequently ignored and the symptoms are attributed to brain damage incident to the trauma or operation. This despite the fact that a fundamental physiologic principle is crying out for recognition, namely, that within the trephined skull the brain pulsates with each change in arterial or venous pressure whereas in the intact skull the brain does not pulsate (3, 6). Therefore when the surgeon leaves a defect in the skull of any significant size he converts a nonpulsating organ into a pulsating one. The effects on the portion of the brain beneath the defect are bound to be significant and the method of progression of the blood flow to the entire organ is necessarily altered.

There is one dictum in surgery that is seldom denied, namely, that immobilization aids wound healing. Since immobilization is important in wounds of bony tissues it should be doubly important in the case of wounds of the brain. But when the surgeon closes the scalp over a brain wound without repairing the cranial defect, he has only has not immobilized the structures, *he has allowed them to remain in a constant state of pathologic mobility*. Furthermore, this state of pathologic mobility does not cease to exist when

From the Cleveland Clinic.

the brain and the scalp wound have healed but persists throughout life or until the bone defect is repaired or the scar has become so dense and inelastic that it no longer pulsates.

A common sequela to brain injury is post traumatic epilepsy. It may occur after a cerebral contusion in the intact skull but is far more common after a penetrating brain wound. All are agreed that it is due to the cerebral scar. But Grant and Norcross found that 18 of 27 patients were improved or relieved of their seizures after an operation in which nothing was done except a repair of the cranial defect. After analyzing the results of cranioplasty in 83 patients these authors concluded that epilepsy is benefited and the syndrome of the trephined is relieved in the large majority of cases by closure of the skull defect. Then may it not be assumed that some of these patients would never develop these symptoms if the skull defect were repaired immediately after the injury?

In the course of certain experiments on the rabbit brain, Falconer and Russell performed a standard decompressive operation in about 270 animals. As a corollary of these experiments they noticed certain pathologic changes in the subcortical white matter beneath the center of the site of operation in about 50 per cent of the animals with the formation of a cavity or cyst in about 30 per cent. These changes appeared to be intimately associated with cerebral herniation and the authors concluded that they had some bearing on the pathogenesis of traumatic cerebral cysts in man. Holbourn explained these lesions by a purely physical consideration of the stresses and strains occasioned by the herniation of cerebral tissue. In my opinion, however, these authors do not attach sufficient significance to the movement of the brain occasioned by the constantly changing intracranial pressure.

The encephalographic finding of 'migration' of the cerebral ventricle toward the site of a traumatic skull defect is familiar to every neurologic surgeon. The foregoing observations of Falconer and Russell suggest that this 'migration' is not due entirely to loss of brain tissue and scar contraction from trauma *per se* but that it is partly due to a progressive gliosis and atrophy of the pulsating portion of the brain beneath the skull defect.

MATERIALS USED FOR CLOSURE

In addition to the failure to appreciate fully the deleterious effects of cranial defects, the neurologic surgeon has been handicapped by the lack of a really suitable material for closure of them. The most widely employed material has been bone or cartilage usually obtained from the patient. This method is traumatizing to the patient as well as time-consuming provided sufficient care is exercised to obtain a good cosmetic result. Recently vitallium has been employed with excellent results. Its only disadvantage is that the implant must be performed since the material is not malleable. With the advent of tantalum it appears that an almost ideal material for closure of cranial defects has been found.

Tantalum is a pure metal with the atomic number 73 in Group V of the periodic table. It has chemical and physical properties which render it very satisfactory for covering cranial defects. First and most important it is biologically inert, a property essential in any material used for bone repair. Second a sheet of tantalum 0.0125 inch (0.3 mm.) thick is firm enough to afford adequate protection over a cranial defect of any size. At the same time, it is sufficiently malleable to be cut and shaped at the operating table with ordinary tin shears and a hammer. These physical properties permit tantalum to be used for closure of defects of the skull either traumatic or surgical without previous shaping of the implant.

LITERATURE

Carney made a survey of metals to find one as inert as vitallium but which could be drawn into wire and worked in the cold state. He selected tantalum because it possessed these latter qualities, and his experiments showed that it was well tolerated by the tissues of the host. In 1940 Burke reported 34 clinical cases in which tantalum wire was found to be an incomparable skin suture. Venable and Stuck (16) stated that passivity or freedom from electroactivity in the body fluids, is an essential quality of any metal for use in the body. Tantalum and vitallium had this quality and stainless steel was "relatively" inert. Venable (15) stressed the fact that a combination of two metals should never be used even though each is inert in itself. For instance a plate of one metal fastened in the host with screws of another metal acts as a destructive battery. Pudenz (10) in 1943 demonstrated the tolerance of brain tissue for tantalum and advocated substitution of tantalum clips for silver clips for hemostasis in neurologic surgery. Pudenz and Odom (12) in searching for a material to prevent meningocerebral adhesions,

found that tantalum foil was better tolerated than was any other material tested. In an experimental study of the repair of cranial defects with tantalum, Pudenz (11) concluded that tantalum was a satisfactory alloplastic material for repair of cranial defects, since it was noncorrosive, inert in tissue nonabsorbable, malleable and lacked toxic ingredients. In 1943 Fulcher reported the first use of a tantalum plate in man for the repair of a cranial defect and suggested that tantalum be used for immediate repair of compound fractures of the skull. He pointed out that, although both tantalum and vitallium were inert materials, tantalum was far better for cranioplasty because it could be shaped and cut at the operating table, whereas vitallium could not. Spurling described a technique for repair of severed peripheral nerves using sutures of tantalum wire and a cuff of tantalum foil around the suture line. He presented gross and histologic evidence to demonstrate that tantalum was inert in human tissues and that scarring and fixation of repaired nerves could be reduced to a minimum by judicious use of tantalum foil.

NOTE: As this article was in preparation, Robertson reported his experiences with tantalum cranioplasty in 26 clinical cases. Fourteen of these cases were simple or compound depressed fractures of the skull, and in 5 of the latter the brain was exposed to the atmosphere for periods longer than 30 hours. Yet, to quote Robertson, "these patients were operated upon and tantalum cranioplasty was done following debridement and sulfonamide therapy without later difficulty." In the same journal DeLancey, Linell, and McKenzie (4) reported on an experimental study on the use of tantalum in the subdural space. They found serious reactive thickening of the dura mater over the tantalum in all dogs, and in many there was a similar but slighter reactive thickening of the underlying arachnoid membrane. These findings are at variance with those of Pudenz and Odom ().

HEALING OF INFECTED EXPERIMENTAL WOUNDS CONTAINING TANTALUM

In order to observe the healing of infected wounds containing pieces of tantalum Dr. Frank C. Boyer and I performed the following experiment. Eight rabbits were selected, anesthetized with intravenous nembutal and the backs shaved. A subcutaneous pocket was made through a skin incision 0.5 inch in length on each side of the back. One-half cubic centimeter of a fresh broth culture of *Staphylococcus aureus* was introduced into each wound. A piece of tantalum sheet 0.5 inch square and 0.0125 inch (0.3 mm.) thick, was then introduced into the subcutaneous pocket on the right side, and both wounds were closed with two silk skin sutures.

Six rabbits survived the experiment. The 6 control wounds in these animals all became in-

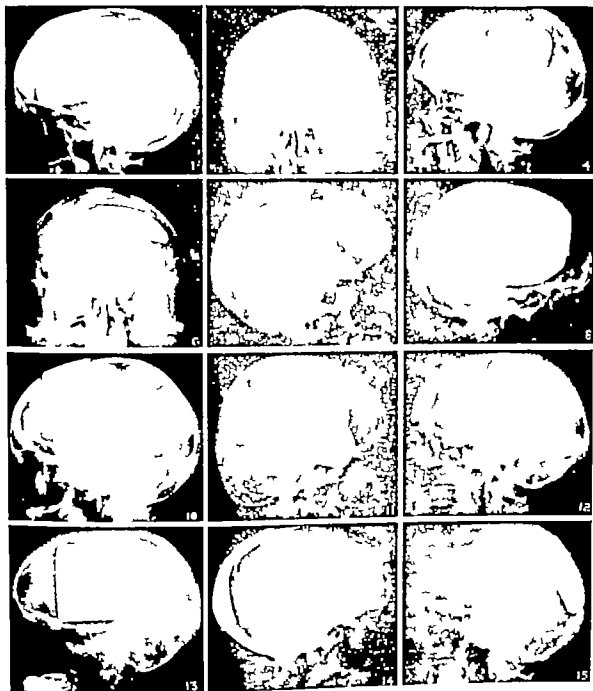


Fig. 1 Postoperative roentgenograms. Numerals are case numbers.

infected. Five of the tantalum wounds became infected, the sixth one remaining healthy. Infection appeared first in the control wounds in 4 instances, first in the tantalum wound in 1 case, and simultaneously in both wounds in 1 case. Infection in each case appeared between the 5th and the 10th day. The wounds were incised and drained between the 10th and the 15th day and all healed between the 19th and the 31st day. In 1 case the tantalum was discharged from the wound. In this rabbit necrosis and sloughing of the skin occurred with the formation of large

ulcers at the site of both wounds. There was no appreciable difference in the rate of healing of the wounds containing tantalum and the controls.

CASE REPORTS

At the Cleveland Clinic tantalum has been used to repair cranial defects in 15 cases (Fig. 1). In 4 cases (1, 2, 3, 13) tantalum was used to cover defects caused by removal of bone invaded by tumor tissue. In 3 cases (4, 8, 10) tantalum was used to repair a defect caused by removal of bone with the rongeur when the original craniot-

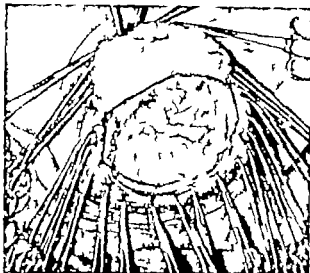


Fig. 2. Case 2. The cranial defect 6 weeks after tantalum cranioplasty. The brain is covered by thin translucent menbrane.



Fig. 2. Case 2. The cranial defect 6 weeks after tantalum cranioplasty. The brain is covered by thin translucent menbrane. b. The second implant in place.

omy opening was not advantageously placed for removal of a brain tumor. In 2 instances (7-11) operations were performed for recurrent brain tumor. The bone immediately over the tumor was removed with the rongeur without attempting to lift the previous bone flap. This shortened the procedure and provided a small but more effective exposure. After removal of the growth the defect was covered with a tantalum implant. In 3 instances (5, 9, 14) tantalum was used to repair an old cranial defect. In 2 cases (6-12) the implant was used for the immediate repair of a compound fracture of the skull. In the remaining case (15) tantalum was used to close the bony defect immediately after the excision of multiple brain abscesses and primary union resulted.

The results in these clinical cases substantiate the findings of earlier investigators regarding the advantages of tantalum for cranioplasty.

CASE. Repair of cranial defect caused by excision of metastatic tumor of the frontal bone. Inadequate traction necessitated second operation. A woman, aged 50 years, had single metastatic lesion in the left frontal bone from malignant adenoma of the thyroid, which had been removed year before. The lesion measured 5 inches in diameter on x-ray films. Operation, as performed on March 9, 1943. A flap of scalp, as reflected, leaving the periosteum attached to the bone. Block removal of the bony tumor was then accomplished with wire saw. Some tumor tissue remained adherent to the outer surface of the dura, which was therefore widely excised.

A roughly circular piece of tantalum 6.30 inch (160 mm.) thick was cut and fashioned with a hammer on concave wooden block to conform to the shape of the skull. The edges of the implant extended about .5 inch beyond the bony margins of the opening. Shallow grooves were cut in

the outer table of the skull to give the edges of the implant some degree of fixation. The scalp was closed over it.

During the postoperative course, the scalp over the implant became distended with fluid, and when the patient leaned forward, the implant slipped forward a short distance. Because the movement of the implant and the accompanying clicking sound annoyed the patient, second operation was performed on April 1. The implant was found to be enclosed in a thin-walled sac, with an inner surface of young translucent dura. A new implant was fashioned from sheet of tantalum .35 inch (.9 mm) thick and was fastened to the skull with two tantalum wire sutures (Fig. 3).

Fluid again collected beneath the scalp for some weeks. It did not require aspiration and eventually subsided. There was no movement of this implant. The thinner material used at the second operation was shaped more accurately and with less effort than that used at the first implant.

When the patient was last seen 4 months later the cosmetic result was excellent. However additional cranial metastases had appeared.

CASE. Repair of cranial defect caused by excision of hemangioma of frontal bone and sinuses. Introduction of tantalum implant into frontal sinuses did not interfere with healing. A woman, aged 55 years, had a hemangioma of the skull 4 inches in diameter which produced an unsightly swelling in the middle of the forehead. Roentgenograms showed extension into the upper half of both frontal sinuses.

Operation was performed on March 8, 1943. A horseshoe-shaped scalp flap was reflected down to the eyebrows leaving the periosteum attached to the bony swelling. The entire thickness of the involved bone including the upper half of the frontal sinuses was removed with the rongeur. The dura was left intact. A roughly circular sheet of tantalum .5 inch (12.7 mm) thick was fashioned to cover the defect. The implant rested on the outer table of the skull to which it was fixed by 4 tantalum wire sutures, with the anterior edge lying on the bony septum separating frontal sinuses just behind their anterior walls. The scalp was closed with single buried tier of interrupted black cotton.

To prevent infection from the nasal passages during convalescence, the patient was given sulfathiazole and was cautioned not to blow her nose. Recovery was uneventful.

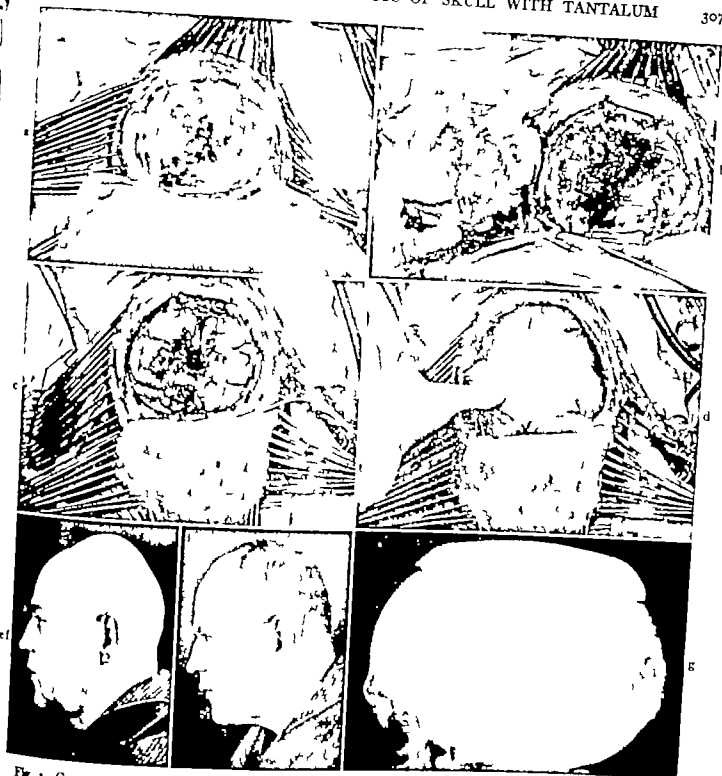


Fig. 3. Case 3. a, The scalp has been reflected showing the tumor of the skull covered with periosteum. b, The inner surface of the bone is invaded by the tumor. c, The meningioma together with the involved dura, sagittal sinus,

and falx has been incised. d, The tantalum implant in place. e, Lateral view of patient before operation. f, Lateral view of patient after operation. g, Postoperative roentgenogram.

and no fluid accumulated over the implant. Three months after operation when a head clamp was tightened in the course of x ray examination of the skull, the patient felt something snap. For 3 months thereafter she occasionally heard clicking sounds in her head. Apparently the tantalum wire sutures gave way under the stress, and the implant occasionally moved.

When the patient was seen 4 months after operation, the cosmetic effect was excellent.

(CASE 3. Repair of large cranial defect caused by excision of bone invaded by parasagittal meningioma. A man aged 45 years, had parasagittal meningioma at the vertex with extensive involvement of overlying bone. On March 9, 1943 the involved calvarium was removed with a wire saw



Fig 4a



Fig 4b

Fig 4 Case 5. Before tantalum cranioplasty b, Six weeks after operation c, Postoperative roentgenogram

leaving a defect 3.5 inches in diameter. The meningoma with the involved dura, sagittal sinus, and falx was excised. A circular sheet of tantalum, .5 inch (0.3 mm) thick and 6 inches in diameter, was fashioned to cover the large bony defect and was fastened to the bone with four tantalum wire sutures (Fig 3). The scalp was closed with a single buried tier of interrupted black silk sutures.

A large amount of cerebrospinal fluid accumulated beneath the scalp flap and was aspirated daily for weeks. The amount of fluid rapidly decreased until aspiration was no longer necessary.

When the patient was last seen, months after operation, the cosmetic result was excellent.

CASE 4. Repair of cranial defect caused by removal of additional bone with rongeur during craniotomy for glioma. Autopsy findings 8½ months later. A man, aged 38 years, was operated upon May 5, 1943. A well circumscribed glioma was removed from the right temporo-parietal region. The dura was closed. After the section of bone was replaced, a piece of tantalum .005 inch (0.3 mm) thick was fashioned to cover a large semicircular defect in the temporal region where additional bone had been removed with the rongeur. For fixation little tongues were cut into the edge of the implant, turned down at right angles, and inserted into small holes bored in the outer table of the skull. The bone flap was secured with tantalum wire sutures. The scalp was closed with a single buried tier of interrupted black cotton sutures. No fluid accumulated in this case. The cosmetic effect was excellent.

The patient returned to work a month after operation. Five months later signs of recurrence of the tumor appeared, and he died on January 1, 1944, 8½ months after operation. At autopsy the tantalum implant was found to be enclosed in a smooth walled, tightly fitting sac which contained no fluid. The outer wall of the sac was about 0.5 millimeter thick and was attached to the under surface of the temporal muscle. The inner wall of the sac consisted of a thinner translucent membrane investing the margins of the bony defect and the outer surface of the exposed portion of the dura. This membrane showed no microscopic evidence of irritation. Where the cortex had been incised for removal of the growth, it adhered in one small area to the dura. The tantalum implant was as smooth and bright as when it was inserted.

CASE 5. Repair of old cranial defect caused by previous excision of left frontal bone for osteomyelitis. A man, aged 30 years, had an operation for osteomyelitis 20 months previously. The left frontal bone was removed including the frontal sinus, supraorbital ridge, and anterior portion of the roof of the orbit. The bone did not regenerate, and the patient asked to have the unsightly defect repaired. He was subject to frequent grand mal seizures.

On June 1, 1943, the scalp incision was reopened, and the scalp reflected from the dura. The perosteum was freed from the margins of the bony opening except here the supraorbital ridge was missing in front. During dissection the dura was punctured in places, and the meningeal membrane of the left frontal sinus was inadvertently opened. A piece of tantalum .5 inch (3 mm) thick was fashioned to cover the defect and perforated with hand punch. The implant fitted snugly without fastening. The scalp was closed over it. During convalescence the patient was given sulfadiazine to combat possible infection from the nasal passages and was cautioned not to blow his nose. Recovery was uneventful, and there was no fluid accumulation. Although the supraorbital ridges were still not symmetrical the cosmetic result was satisfactory (Fig 4). When last heard from 3 months after operation, he had suffered no more convulsive seizures.

CASE 6. Immediate repair of cranial defect from compound comminuted fracture of the skull with laceration of the brain. While endeavoring to remove a heavy tire, a young man, aged 24 years, was struck in the midfrontal region by the run of truck wheel. He sustained a compound comminuted fracture of the skull with laceration of the brain and dura. He was not rendered unconscious immediately but lost consciousness within an hour and had a series of five generalized convulsions.

On June 1, 1943, 14 hours after injury he was operated upon under pentothal anesthesia. The margins of the linear scalp wound were trimmed and retracted, and fragments of loose bone were removed, leaving a bony defect measuring by 5 inches. Lacerated brain tissue was removed by gentle irrigation and suction, and a bleeding point on the cortex was controlled by electrocoagulation. The lacerated dura and sagittal sinus were not bleeding and were not disturbed. A piece of tantalum .5 inch (0.3 mm) thick was fashioned to cover the bony defect and was

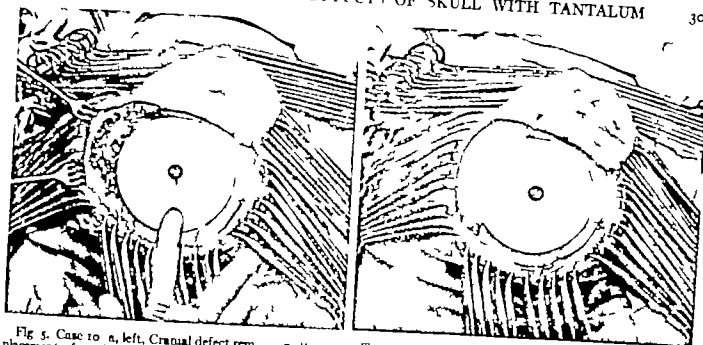


Fig. 5. Case 10. a, left, Cranial defect removed by craniotomy. b, right, Placement of section of bone removed by craniotomy.

The tantalum implant fastened by means of two tantalum screws.

simply laid on the outer table of the skull and the wound was closed with a single buried tier of interrupted black cotton sutures. No drainage was used. Oral administration of sulfadiazine was begun the next day.

The wound healed quickly without fluid accumulation and the patient was discharged free from symptoms on the 12th postoperative day. He resumed work as a truck driver within 2 months. He was last seen 9 months later. He had lost no time from work and the cosmetic result was good.

CASE 7. Repair of cranial defect caused by operation for recurrent glioma. Reoperation 11 months later. A man aged 31 years, had a left parietal glioma removed 6 years previously. She had symptoms of recurrence and disclosed a large calcified tumor of the left parietal lobe.

Operation was performed on August 16, 1943. Instead of elevating the large bone flap of the previous operation, the skull overlying the growth was removed with a rongeur. The tumor was then excised. The lateral ventricle was widely opened during dissection of the growth. The dural defect was not repaired. The cranial defect was covered with a perforated sheet of tantalum 0.025 inch (0.3 mm) thick held in place with two tantalum wire sutures.

Fluid accumulated between the scalp and the implant for 23 days and was removed by daily aspiration or lumbar puncture. The fluid no longer accumulated when the patient was able to be out of bed. She was discharged 28 days after operation.

Ten months after operation symptoms developed suggestive of a recurrence of the growth. Another operation was performed on July 22, 1944. The scalp over the implant was fluctuant. An aspirating needle encountered clear very faintly xanthochromic fluid between the scalp and the implant. This fluid contained no cells, and the total protein content was 245 milligrams per 100 cubic centimeters. A flap of scalp was reflected to uncover the implant, and this maneuver was accompanied by a gush of fluid. The under surface of the scalp was not adherent to the implant but was covered with a smooth, thin membrane. The implant was clean and shining and only loosely anchored by tantalum sutures. The sutures were divided, and the implant was removed. There was no membrane beneath the implant but a huge cavity which proved to be

an enormously dilated left ventricle. The foramen of Monro was not patent. The recurrence of symptoms was thought to be due to obstruction of the ventricle rather than to recurrence of the tumor. The choroid plexus in the obstructed ventricle was treated with electrocautery after which the implant was replaced and fastened with tantalum sutures and the scalp was closed. When the patient was discharged on the 10th day after operation, the symptoms subsided. There was a very slight amount of fluid over the implant.

CASE 8. Repair of cranial defect occasioned by removal of incorrectly localized meningioma. Fixation inadequate. A woman, aged 43 years, presented symptoms of tumor of the left temporal lobe. Operation was performed on August 27, 1943. A circular section of bone over the temporal lobe was removed with a craniotome. The tumor was located much farther forward than was anticipated and most of the left frontal bone had to be removed with a rongeur in order to expose it. After a long, difficult operation accompanied by severe blood loss and surgical shock, a very large meningioma (245 gm., 13 by 7 by 7 cm.) was excised which had originated on the anterior portion of the falx. The section of bone was replaced and fastened with a tantalum suture, but an enormous defect in the frontal bone remained. A piece of tantalum 0.025 inch (0.3 mm) thick was laid across the defect and the scalp was closed over it. The dura was only partially closed. An attempt was made to fix the implant. It was not anticipated that the implant would stay in proper position but it was hoped that it would render subsequent repair easier. The patient had a very stormy convalescence complicated by serious decubitus ulcers, which prolonged the hospital stay to 8 weeks. Large quantities of fluid were aspirated from beneath the scalp every day at night for the first 6 weeks. On one occasion culture of this fluid revealed *Staphylococcus albus*. It was believed that this patient had *Staphylococcus albus* meningitis, which responded to the administration of sulfadiazine.

When the patient was last seen, 35 months after operation, the implant was well fixed but was located about 3 centimeters posterior to its original position, leaving a defect in the left frontal region just below the hairline. The patient wishes to return for repair of this defect, which will

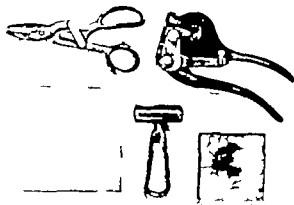


Fig. 6. Author's equipment for cutting, shaping, and perforating the implant: tin shears, metal punch, tantalum plate (6 by 6 inches) round headed hammer, concave wooden block.

probably be closed with another strip of tantalum, leaving the original implant in its present position.

CASE 9. Repair of old cranial defect caused by removal of meningioma. Screw fixation of implant. Death from meningitis secondary to pre-existing dermatitis. A man, aged 54 years, had a very large left parietal defect caused by removal of parasagittal meningioma 4 months previously. At that time it had been impossible to replace the bone flap because of brain swelling. When the patient's scalp was shaved in preparation for cranioplasty, he was found to have dermatitis. The infection was treated for 6 days, and operation was performed on October 8, 1943. The scalp flap was reflected, the margins of the bony opening were exposed, and a piece of tantalum was fashioned to cover the cranial defect. Three tantalum screws were used to fasten the implant to the margins of the bony opening, and the wound was closed. Because of the previous unhealthy condition of the scalp, the patient was given sulfadiazine by mouth. On the 8th day of convalescence he had a convulsion followed by a rising temperature and collection of fluid beneath the scalp. He died 6 days later of fulminating *Staphylococcus aureus* meningitis despite intensive sulfonamide therapy. Death was attributed to an error in judgment in not treating the dermatitis for sufficiently long period before operation.

CASE 10. Repair of cranial defect caused by removal of additional bone with rongeur to expose meningioma. Screw fixation of implant. A man, aged 57 years, presented symptoms of tumor in the right sensorimotor area. On December 8, 1943, circular section of bone was removed with a craniotome, and meningioma was disclosed, which extended beyond the anterior edge of the bony opening. Additional bone was removed with rongeur in order to uncover the growth entirely. The tumor was removed and the section of bone was replaced. The large dural defect was not repaired. A strip of tantalum was fashioned to cover the bony defect and perforated with hand punch. While the assistant held the implant in position, the operator drilled two holes in the skull through the previously selected perforations in the upper and lower margins of the implant. Into these holes were placed tantalum screws, which drew the implant tightly against the outer table of the skull, providing very firm fixation (Fig. 5). The scalp was closed with a single buried tier of interrupted black silk sutures. The patient was discharged on the 3d postoperative day. The cosmetic result, as excellent when he was last seen 7 months after operation.

CASE 11. Repair of cranial defect resulting from operation for recurrent glioma. Screw fixation of the implant. A lad, aged 3 years, had recurrent cystic astrocytoma of the right temporal lobe. At operation on January 26, 1944, instead of re-elevating the previous bone flap, which was not advantageously placed, a large opening was made with the rongeur in the right temporal region through linear incision. After removal of the tumor the dura was loosely closed, and the bony defect was covered with perforated tantalum implant. The implant was fastened to the skull by means of two tantalum screws. The wound was closed with two buried tiers of black silk sutures. During convalescence fluid was prevented from collecting beneath the scalp by means of light pressure with an elastic bandage. The patient was discharged on the 10th postoperative day. When last seen 3 months later the cosmetic result was excellent.

CASE 12. Immediate repair of cranial defect in gunshot wound of the brain. Screw fixation of implant. A woman, aged 34 years, was struck in the right frontal region with a .38 caliber bullet. She was not unconscious, and there was no paralysis or convulsion. X ray showed defect in the frontal bone above and to the right of the frontal sinuses. Particles of lead and bone outlined tract leading deep into the right frontal lobe.

Operation was performed on February 8, 1944, 7 hours after injury. The patient was anesthetized with sodium pentothal. Removal of the emergency dressing disclosed masses of extruded necrotic brain tissue concealing the wound. The scalp was shaved and cleaned revealing wound of entrance and wound of exit separated by bridge of skin 5 inch wide. The bullet had apparently glanced. The bridge of skin was divided, the edges trimmed, and the wound lengthened by an incision at both ends. The wound was irrigated with saline, and quantity of material brain tissue, clot and bone fragments was removed from the bullet tract with an aspirator. The bony defect was enlarged with rongeur so that bleeding points in the brain and dura could be adequately controlled with electrocautery. The defect measured by inches. A small quantity of sulfanilamide crystals was dusted on the lacerated brain. A piece of tantalum 5 inch (3 mm) thick, as shaped, perforated, and placed over the cranial defect. A single tantalum screw was used to fasten the implant to the outer table of the skull. The scalp was closed with buried tier of interrupted black silk sutures in the galea and two superficial sutures in the skin. The patient was given plasma transfusion during the operation. Oral administration of sulfadiazine was begun the next day.

The wound healed rapidly without evidence of inflammation. Convalescence was uneventful, and the patient left the hospital on the 12th postoperative day. The cosmetic result was excellent. She showed no emotional reaction to the tragedy in which she lost her family and almost lost her life. This symptom was attributed to the damage to the right frontal lobe. She resumed her job 10 or 12 weeks after the accident and has remained ill to date.

CASE 13. Repair of cranial defect caused by removal of epidermoid of skull. Screw fixation of implant. A man, aged 5 years, had an epidermoid of the anterior portion of the left parietal bone for 3 years. The defect on the x ray film measured 4 centimeters in diameter. Removal as indicated because of prominent external swelling.

On February 8, 1944, flap of scalp was reflected including the upper portion of the temporal muscle. The lesion was removed in one piece with Hudson drill and wire saws. The dura was not incised. A sheet of tantalum 5 inch (0.3 mm.) thick and 9 centimeters square was fashioned to conform to the shape of the skull. The implant was perforated, placed over the cranial defect, and

fastened to the skull with three tantalum screws. The scalp was closed with a single buried tier of interrupted black silk sutures. Because of the relaxed condition of the scalp covering the implant, a postoperative hematoma developed between the scalp and the implant. By the 27th postoperative day this clot had largely liquefied, and it was removed by aspiration. When the patient was last seen 3 months after operation, the cosmetic result was excellent.

CASE 14. Repair of old cranial defect. A male aged 34 years, with a cranial defect over a porencephalic cyst in the right parietal region. The cranial defect was said to have existed after a severe injury to the back of the head at the age of 7 months. The patient was subject to frequent convulsions.

On March 22, 1944, the scalp was reflected and the cranial defect was enlarged with a rongeur. The entire portion of the dura with the attached cerebral cortex was excised. A piece of tantalum 0.035 inch (0.3 mm.) thick was fashioned to cover the defect, perforated at its center to the outer table of the skull with three tantalum screws. The scalp was closed with a buried tier of interrupted black silk sutures. Fluid collected between the implant and the skull removed daily either by aspiration of the spinal puncture. After the 5th postoperative day the accumulation was controlled by light pressure elastic bandage. The patient was discharged 14 days after operation. When last seen 15 weeks after operation, the result was good and there had been no further convulsions.

CASE 15. Repair of cranial defect after multiple brain abscesses. Primary healing of infection. A young man, aged 17 years, was hospitalized after a frontal craniotomy for osteomyelitis of the frontal bone complicating frontal sinusitis. During this time he had repeated operations for the drainage of brain abscesses in the left frontal and right occipital lobes. The organism was a penicillin sensitive anaerobic streptococcus. On June 1, 1944, the patient was extremely ill with meningitis and multiple brain abscesses in the right parieto-occipital region. On this date a flap of scalp was reflected and a bony opening 2.5 inches in diameter was made over the site of the abscesses. The dura was excised, and the diseased brain was cut away with the electro-surgical loop to a depth of more than 2 inches. Several small subcortical abscesses were opened and removed. Palpation then disclosed a large firm subdural abscess plastered against the right side of the falx. This was incised and about 2 ounces of thick pus escaped. The outer wall of this abscess was excised and the medial wall was left attached to the falx. Ten cubic centimeters of penicillin solution, 1000 units per cubic centimeter, was introduced into the cavity in the brain tissue, after which a perforated tantalum implant was placed over the bony opening and fastened to the outer table of the skull with two tantalum screws. The scalp was then tightly closed with a buried tier of interrupted black silk sutures in the galea. Drainage was not instituted, and the wound was not aspirated. For the next 48 hours the patient received 10,000 units of penicillin every 4 hours intramuscularly, 10,000 units every 4 hours was injected beneath the scalp over the tantalum plate, and 10,000 units was given intrathecally every 12 hours. After 48 hours the intrathecal injections were discontinued, and the injections beneath the scalp were reduced to twice a day. The intramuscular injections were continued until the 16th postoperative day. The temperature reached normal on the third day after operation and remained normal.

Convalescence was very smooth and the patient was discharged 3 weeks after operation. At no time was there any evidence of inflammation in the wound. When last

seen 2 weeks after operation he was free from symptoms and the cosmetic result was good.

As the result of experience with 15 cases reported it appears that tantalum is an almost ideal material for the repair of cranial defects. It can be used to repair either surgical or traumatic skull defects, whether they are fresh or old. A sheet of tantalum 0.025 inch (0.3 mm.) thick is sufficiently rigid to afford adequate protection over a cranial defect of any size yet it can be readily shaped at the operating table to conform to the contour of the skull. The necessary implements are a pair of tin shears, a metal punch, a round headed hammer and concave wooden block (Fig. 6).

Small tantalum screws provide the best method for fastening the implant to the skull. In addition to providing perfect fixation they permit the operator to draw the edges of the implant down against the skull and thus save time which would otherwise be spent in meticulous shaping of the implant to the contour of the skull. Unfortunately tantalum screws of the proper size are not yet in the market. Those used in the cases described were made by hand.

In these 15 cases there were 7 instances of large unprepared dural defects beneath the implant. In 1, 4, 7, 9, and 13 significant collections of cerebrospinal fluid developed between the scalp and the implant which persisted for some weeks, apparently until the newly formed dura became watertight. The fluid collection in no case prolonged the patient's hospital stay nor did it impair the final result. In later cases the accumulation of fluid was controlled by a few turns of elastic bandage over the dressing. Perforating the implant had no effect on the frequency of occurrence or the duration of fluid collection. This accumulation of fluid could probably be decreased or perhaps prevented entirely by closing the dural defect with a dural substitute. However in my opinion it is better to accept this fluid accumulation and treat it by using an elastic bandage or by aspiration while the new dura forms rather than to place another extraneous material next to the brain. The accumulation of cerebrospinal fluid over the implant is not an irritative phenomenon. It occurs because the scalp is not adherent to the smooth surface of the implant and therefore the cerebrospinal fluid pressure lifts the scalp away from it.

There was one infection in this series of 15 cases and it resulted in the patient's death. It was due to an error in judgment in operating soon after a

(Since completion of this article it has been announced that tantalum screws for skull plates will be obtainable on or about April 1945.)

TABLE I—CASES RECEIVING PROTEIN DIGEST

Disease	N. of patients
Ruptured diverticulum of the colon with peritonitis	1
Ruptured liver with peritonitis	
Ruptured appendix with peritonitis	3
Carcinoma of the stomach with gastric resection	3
Peptic ulcer with gastric resection	
Intestinal obstruction	5
Cholecystitis	4
Appendicitis with appendectomy	4
Tuberculous peritonitis	3
Stab wound of the abdomen	
Gunshot wound of the abdomen	
Acute pancreatitis	1
Pelvic abscess	
Abdominal abscess	
Rectal fistulas	
Perforated peptic ulcer	1
Burns	3
Hemorrhoids	
Multiple lacerations	
Inguinal herniorrhaphy	
Strangulated inguinal hernia with repair	
Papillary cyst adenoma with hypoproteinemia	
Cirrhosis of the liver with hypoproteinemia	
Intestinal fistulas	
Carcinoma of the descending colon and intestinal obstruction	
Carcinoma of the transverse colon and intestinal obstruction	
Lymphopathia venereum with combined abdomino-perineal resection	
Bulbar polypionitis	
Safety pin in duodenum with duodenostomy	
Abdominal eversion	
Total	49

intravenously during this study was 165.5 liters.

In view of the nitrogen content, 1 liter of the protein digest solution contains approximately 6.25 grams of nitrogen or is equivalent to approximately 60 grams of protein. Thus the administration of 1 to 3 liters a day would give a patient the equivalent of 60 to 180 grams of protein. One patient in this study who received 21 liters in 21 days, received the equivalent of approximately 1260 grams of protein. This is a large secondary supply to give an acutely ill patient whose intake is markedly limited. The use of such protein digest intravenously has an important sparing action upon the body proteins which are drawn upon when the need is great and the intake is inadequate.

Rate of administration. The average time required for the injection of 1000 cubic centimeters was 95 minutes, the shortest time being 43 minutes and the longest time being 149 minutes. The average rate of injection was approximately 10.5 cubic centimeters per minute or about 140 drops per minute. This rate would be equivalent to the administration of approximately 0.0655

TABLE II.—REACTIONS

Type of reactions	N. of reactions
Type Systematic	
Face flushed	
Feeling of warmth	(same patient)
Nausea	
Vomiting	
Type Pyrogenic	
Shaking chill	
Slight elevation in temperature	
Change in pulse rate	5 (4 patients)

grams of nitrogen equivalent to 0.63 grams protein digest per minute or approximately 37.8 grams of protein digest per hour. We have found that the giving of 100 cubic centimeters of solution at a rate less than 10 cubic centimeters per minute results in a moderate amount of physical discomfort to the patient because of the length of time required for the administration.

Reactions. In 200 consecutive intravenous infusions of the protein digest solution there were 7 reactions equivalent to 3.5 per cent. These reactions are classified in Table II.

A detailed analysis of the reactions follows.

Type Reaction. The patient was white female who had a duodenal obstruction caused by safety pin. The protein digest solution (Batch No. BW 5 C) as given on the first postoperative day. The injection was started at rate of 60 drops per minute. After receiving 300 cubic centimeters of the solution, the patient complained of nausea and feeling of warmth. Her face was flushed and her skin was rather warm. The rate was decreased to 30 drops per minute and the symptoms subsided. At 400 cubic centimeters the patient vomited. However she had been vomiting during the morning prior to the administration of the protein digest. This vomiting was not forcible but as characteristic of the type frequently seen after operation. The injection was continued until 500 cubic centimeters had been given. Throughout the last 100 cubic centimeters, there were no objective manifestations in the patient.

Type Reaction. This reaction occurred on the following day in the same patient. The solution was from the same batch (N. BW 5 C) used on the previous day. The fluid was started at 60 drops per minute. After 50 cubic centimeters had been administered, the patient complained of feeling hot. When the rate was slowed to 30 drops per minute, the symptoms decreased somewhat but not completely. She vomited after 50 cubic centimeters had been given, but the injection was not stopped and as slow as to flow at rate of 30 drops per minute with very little discomfort to the patient. As on the previous day the patient had been vomiting prior to the intravenous injection.

Type Reaction. This patient was colored male who had right inguinal herniorrhaphy. The protein digest was given to him on the second postoperative day and was taken from Batch N. BW 6 C. The injection was started at the rate of 60 drops per minute and after receiving 300 cubic centimeters the patient complained of numbness in the arm being used. He then developed a shaking chill which lasted about 5 minutes. The fluid was not discontinued and the remaining 300 cubic centimeters

of solution in the bottle was given. At no time did the patient complain of feeling warm or was there any change in the appearance of the skin. There was no change in temperature. This patient was extremely apprehensive about receiving fluids intravenously.

Type 2 Reaction 2 This colored patient had been subjected to an inguinal herniorrhaphy on the same day as the patient in Reaction 1. He was in the same room with the latter and saw him have the chill. He was given the solution from Batch BW61C, the initial rate being 60 drops per minute. After receiving 450 cubic centimeters a chill developed. The injection was stopped for a few minutes and then restarted at 160 drops per minute until 500 cubic centimeters had been given. The chill lasted only a few minutes and there was no change in temperature. There was no actual shaking but only a feeling of chilliness. This patient had become very nervous after seeing the other patient experience the reaction.

Type 3 Reaction 3 This patient was an elderly white female who was critically ill with severe hypoproteinemia, edema, and a papillary cystadenocarcinoma with metastasis in the abdominal cavity. The first infusion of the protein digest solution from Batch No. 102 was given at 10 drops per minute and 1 liter was injected. Forty minutes after the infusion had been completed the patient had a shaking chill which lasted about 10 minutes. There was a rise in temperature from normal to 101 degrees. She vomited all day but had been vomiting before the infusion. This patient received 10 other infusions of 1 liter each at the same rate and from the same batch, No. 102 of material on 10 consecutive days without showing any further reactions.

Type 2 Reaction 4 This was a colored female with a carcinoma of the descending colon with obstruction. A colostomy had been performed. Practically no food could be taken by the oral route. She was given numerous infusions of the protein digest solution. A reaction occurred with the twelfth consecutive infusion of 500 cubic centimeters of solution from Batch No. 102. The patient was critically ill at the time. The injection was started at the rate of 160 drops per minute and after receiving 500 cubic centimeters, the patient complained of feeling chilly. The chill lasted for nearly an hour but the severity decreased a great deal during the last 45 minutes. Throughout the chill and for some time after the patient was given another 500 cubic centimeters of the protein digest solution (No. 102) at 60 to 80 drops per minute. At the end of the infusion the patient felt normal and there was no further reaction. There was no change in the color or warmth of the skin throughout the reaction. The same tube and needle set was used throughout the injection of 1000 cubic centimeters of solution.

Type 2 Reaction 5 This reaction occurred in the same patient as described in Reaction 4. The solution used was also from Batch No. 102. The injection was started at 40 drops per minute. After having received 450 cubic centimeters, the patient began to have a rather severe chill and the pulse rose from 98 to 115. The infusion was then stopped. The chill lasted 45 minutes. At the end of the chill another 500 cubic centimeters of the same lot of solution was given at the rate of 140 drops per minute, a second tube and needle set being used. There was no reaction with the second 500 cubic centimeters. The patient received 8 other 1000 cubic centimeters infusions of the same lot of material without reaction.

In all there were 7 reactions in 200 consecutive infusions of the protein digest solution. The first two reactions on one patient we have classified as

being due to substances present in the preparation which caused a vascular reaction with flushing of the skin, a sense of warmth, and nausea with vomiting. However since this patient had been vomiting prior to the intravenous administration of the protein digest solution there is some doubt as to whether the vomiting may be attributed to the solution. As has been noted the vomiting was characteristic of that frequently seen after operation. There were 34 other infusions with the same material in different patients at rates varying between 160 and 120 drops per minute with no reactions.

Reactions of type 2 including reactions 1 to 5 were due chiefly to pyrogenic substances present in the tube and needle set and were not inherent in the solution used. It will be noted that in all these reactions the patients experienced chills. There was only an occasional associated change in temperature and pulse rate. In no instance in this type of reaction was there any flushing of the skin, nausea, a feeling of warmth or vomiting which could be attributed to the solution as in reactions of type 1. The statement that the pyrogenic reaction was undoubtedly due to an improperly prepared tube and needle set seems to be borne out.

In reaction 3 type 2 it will be noted that this patient subsequently received 10 other infusions on 10 consecutive days without showing reactions. A similar explanation may be given for the reaction experience in reaction 4 type 2. The fact that the same set was used for the administration of the second 500 cubic centimeters infusion which was given without reaction would indicate that the first lot of 500 cubic centimeters had washed out the pyrogenic materials from the tube and needle set.

In reaction 5 it is clearly shown that the pyrogenic reaction was due to the improperly prepared tube and needle set since the second lot of 500 cubic centimeters of the same batch was given at the same rate without reaction when a second tube and needle set were used. Subsequently the patient received 8 other infusions of the same lot of material without any reaction.

During the entire study close observation of the local reaction resulting from the intravenous use of the protein digest solution has never revealed any acute thrombophlebitis. We have noticed that after many infusions in the same arm there was a gradual increase of thrombosis in these veins. However the same veins were also used for the infusions of other parenteral fluids such as glucose and normal saline solutions. In one case, there was an extravasation of protein digest solu-

fied as systemic reactions or 2.5 per cent occurring in 4 different patients have been attributed to pyrogenic substances present in the tube and needle set. A discussion of the reactions is presented.

4. No acute thrombophlebitis was observed as being due to the injection of the protein digest solution.

5. The protein deficit which exists in surgical patients after operation has been performed is pointed out. The value of the use of a digestible and assimilable protein intravenously in order to supply this protein deficit so as to avoid a negative protein balance which drains the body and plasma proteins is discussed. A few cases are presented which exemplify the efficacy of this protein digest.

6. This protein digest solution may be safely used in critically ill surgical patients as a simple method of supplying a source of parenteral protein.

7. It is possible that in some cases, the addition of vitamins, glucose and inorganic salts may be advantageous.

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PRACTICAL CONSIDERATIONS IN DEFINITIVE AMPUTATION SURGERY

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IN this discussion we wish to emphasize certain technical procedures which have been found helpful in securing painless well shaped useful stumps in lower leg thigh forearm and arm amputations. Specialized technical procedures such as fusion of the fibula to the tibia lengthening operations and removal of the fibula will not be considered. Also for the sake of simplicity the well known and often discussed amputations—Lisfranc, Chopart, Pirogoff, Syme, Callander, disarticulation and Gritti Stokes—will be omitted.

When the dressings are removed from patients with amputations who arrive for definitive surgery at a general hospital and a well performed guillotine amputation with adequate skin traction is disclosed there is a silent word of thanks to the surgeons at the Front because the problem of definitive surgery has been greatly facilitated and the success or failure of securing the best possible stump rests firmly upon us.

An amputee is keenly interested in a good result. This type of surgery is always under the close surveillance of the patient himself. He compares his stump as to comfort, appearance and function with those of other similar cases, and sets up his own standard for a good result which stands little correction. It is interesting to note that many, within a few hours after they arrive at the general hospital, have by some method found their way to the brace shop and the physical therapy department, have talked with other patients in similar circumstances, and have formulated definite opinions about the amputation center in general. Therefore the surgeon must not only obtain the maximum in shape and function for the prosthesis maker and for his own personal satisfaction but for the general morale on his service.

GENERAL CONSIDERATIONS

The anesthesia used at Bushnell General Hospital for lower extremity amputation surgery has generally been spinal for forearms, brachial blocks for upper arms, inhalation or intra-

venous pentothal sodium. It is essential to select an anesthetic that allows sufficient time for all the intricate details including absolute hemostasis.

Whenever possible the surgery is done with a tourniquet in place until the amputation has been performed and flaps have been fashioned ready for closure. The extremity is elevated and bled by tightly applying ace bandages from the distal end to the site selected for the tourniquet. The tourniquet itself may consist of the usual rubber commercial type, multiple ace bandages (3) one over the other or in upper extremities a blood pressure cuff with a superimposed ace bandage.

Nerves are treated with 20 per cent formalin¹ tinted with methylene blue injected between two ligatures approximately 1 centimeter apart which insures an equal diffusion of the solution throughout all nerve fibers in this segment. After a few seconds the proximal ligature is removed and the nerve transected just distal to the remaining ligature care being taken that the nerve end is high in normal tissue away from the line of closure. It is realized that the various methods of treating these sectioned nerves are controversial. Injection of 95 per cent alcohol is utilized by many surgeons with good success and it is highly possible that the many advocates of simple nerve division without ligation or any injection may prove to have the best method.

The suture material has been cotton Nos. 40-80 for deep fascial approximation, 120 for ties and subcutaneous and C. Deknatel silk for skin closure. All stumps are closed snugly without drainage.

PREPARATION

Extremities to be revised or reamputated should be free of open draining wounds or granulating areas¹ except in a few instances in which the selected site for reamputation is well away from the open area. The waiting period after the stump has become dry is in proportion to (1) the length of time the stump had drained, (2) the depth of the wound which was draining and (3) the type of organisms that were present during the healing period. For example a guillotined

¹From the Orthopedic Section of the Surgical Service, Bushnell General Hospital, Brigham City, Utah.

²This is the practice at Bushnell General Hospital and must not be interpreted to be that common to all Army amputation centers.

stump with adequate skin traction that heals rapidly and becomes dry in 4 to 8 weeks may be operated upon in 14 to 21 days after becoming dry, provided the scar can be removed *en bloc*. An indolent healing amputation that has contained sinus tracts, ring sequestra, foreign material, or organisms of high virulence etc. and in which revision or reamputation is contemplated in the immediate vicinity of the scarred end should remain dry 30 to 60 days before definitive surgery is carried out. Often if we wish to close a granulating stump rapidly to shorten the waiting period, our plastic surgeons have been prevailed upon to place several pinch grafts¹ on the open end to speed the healing time. In some instances the reapplication of skin traction has hastened the period of healing as well as relaxed the skin for revisions near the guillotined end. Attempts to hasten matters by reamputating before complete closure have proved unwise in our hands.¹ Certainly the methods advocated in this paper are not all applicable if reamputations are done in the presence of such likelihood of contamination.

At present we are treating with intramuscular injections of 15,000 to 25,000 units of penicillin every 3 hours a comparative group of patients from whose wounds cultures show penicillin sensitive organisms. The operation is then done as soon as the wound becomes dry or the culture from the wound sterile (usually in about 5 to 7 days) and penicillin therapy is continued for 7 to 10 days after operation. Results of this method are not conclusive at this time.

Except in the penicillin group all patients are prepared for 2 or 3 days with sulfadiazine, grams 1, given once every 4 hours and a booster dose of tetanus toxoid before surgery and sulfadiazine continued after operation for 10 to 15 days unless contraindicated. The amputated member is shaved, cleaned with green soap, alcohol, ether and wrapped in sterile dressings the afternoon of the day preceding the operation.

AMPUTATIONS BELOW THE KNEE

If a guillotine amputation has been done in the lower third of the leg, a site for the level of division of the tibia is selected between 5 and 7 inches from the tibial table. This level is marked around the leg on the overlying skin, with methylene blue. Our desire is to have the line of skin closure posterior to center. Flaps are accurately measured by first estimating the anteroposterior diameter of the leg at the level selected for amputation of the tibia. This diameter can be measured by

placing a short rule by the leg and sighting, or it can be more accurately determined by measuring the circumference of the leg and dividing by three. We utilize two-thirds of this diameter for the length of the anterior flap and one third for the posterior. A methylene blue mark is therefore made on the skin anteriorly below the level for amputation of the tibia at a distance two-thirds of the diameter. Posteriorly the mark is made at a distance one third of the diameter. An anterior and posterior skin flap is then plotted with methylene blue from these established levels. Since the skin will retract when the anterior flap is cut, the distance from the bone level selected for amputation to the distal part of the anterior flap is measured accurately and the tibia is scored at the distal level when the skin incision is first started anteriorly. After the skin flap has been reflected this measurement can then be plotted on the tibia itself and the site of amputation permanently established with a chisel mark. The establishment of a stationary mark for amputation for reference in fashioning skin and fascial flaps as well as for trimming muscles is important and time saving as the shifting of skin and other structures due to retraction or steadying of the limb by an assistant may cause the surgeon to section the tibia at a higher or lower level than anticipated thus necessitating a revision of his planned procedure.

A long posterior fascial flap is then fashioned and cut except in its distal posterior aspect, the medial and lateral portions being dissected free so they may be retracted to avoid injury when the amputation knife is carried under the tibia and fibula. A $\frac{1}{4}$ inch anterior fascial collar is prepared care being taken to separate the fascia where it is closely adherent to the periosteum of the tibia without lifting the tibial periosteum. The fibula is approached through the posterior lateral muscular raphe between the peroneus longus and the soleus and dissected free of its attachments extraperiosteally to a level approximately 1 inch shorter than the selected site of amputation. The anterior tibial artery and its plexus of veins should be identified and ligated through this approach, thus avoiding unnecessary bleeding when the tourniquet is released. At this level the periosteum is ringed and stripped distally. A Gigli saw is passed around the fibula, and the bone cut transversely about $\frac{3}{4}$ inch distal to the proximal periosteum. We do not remove the muscles at the level of the fibular amputation but divide them at the level selected for the amputation of the tibia. This muscular tissue fills the defect left by the removed fibula and keeps the stump end straight (Fig. 1).

¹This is the practice at Eisenhower General Hospital and must not be interpreted to be the custom in all Army amputation centers.

The posterior fascial flap is made very long and free of attached muscle below the level of division of the tibia. In forming this fascial flap we rotate the fibula anteriorly to the level of the tibia, insert the blade just behind the bones, divide all muscle fibers perpendicularly taking care to avoid any incision into the fascia. The knife is then turned parallel to the posterior border of the tibia, carried distally anterior to the gastrocnemius fascia and cut across at the desired low level. The periosteum of the tibia is rimmed with a knife at the site of amputation including the anterior bevel and stripped distally. The tibia is sawed about $\frac{1}{4}$ inch distal to the periosteal collar. The distal segment is discarded and the vessels and nerves can be plainly seen and ligated. The gastrocnemius fascia is cleaned of any remaining muscle. We wish to stress the point that in carrying the line of dissection of the posterior muscles obliquely downward resultant redundancy in the posterior aspect of the stump is avoided (Fig. 1).

With the hand placed under the leg near the amputated end and with slight pressure upward the bulge of gastrocnemius muscle will be seen on the medial aspect of the tibia. A wedge of this muscle is removed to insure a straight stump (Fig. 1). The tourniquet is now removed and absolute hemostasis is established. Fascial flaps and skin are then closed under slight tension. We have adopted a dressing consisting of voluminous gauze fluffs or mechanics waste held by an ace bandage or sheet wadding and a light plaster cast applied over all to the upper third of the thigh with the knee in full extension. Twenty-four to 48 hours later the cast is bivalved and the lower half is used as a posterior mold until the incision is healed (Figs. 2 and 3).

AMPUTATIONS OF THE MIDDLE AND LOWER THIRD OF THE THIGH

In considering definitive surgery on guillotined thighs it is of prime importance to save as much length as possible. Re-establishment of skin traction 5 days before surgery will often forestall shortening of the femur. The scar is removed *en bloc* and if severe spurring is present at the femoral end a distal segment of the bone is removed with the scar. The skin flaps are planned and marked much the same as in lower leg amputations with a long anterior and short posterior flap. The skin is reflected and anterior and posterior fascial flaps prepared by utilizing all nonscarred fascia. The bone end is treated by removing a $\frac{1}{4}$ inch periosteal cuff or if it is well covered with deep fascia and no spurring has occurred it is not disturbed.

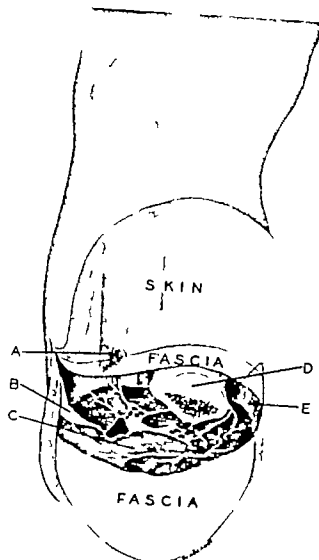


Fig. 1 shows the tibia which was approached through the intermuscular raph *B* and cut about 1 inch short than the tibia. *C* illustrates the muscles cut transversely at the level of amputation. *D* represents the beveled tibia. *E* denotes the segment of gastrocnemius muscle to be removed before closure.

A generous wedge of muscle is removed from the region of the vastus medialis and vastus lateralis and the quadriceps femoris is thinned near the amputated end of the femur. No muscular attachments should be disturbed proximal to the femoral end. The removal of these segments of redundant muscle tapers the stump, facilitates proper shrinkage, makes for better fitting prostheses and often supplies the needed fascia and skin necessary to forego shortening the femur. Here again absolute hemostasis is required before closing the wound. In approximating the fascial and skin flaps it is well to put slight transverse tension on the lower flaps to avoid longitudinal folds in the posterior thigh when shrinkage of the stump occurs. The initial postoperative dressing consists usually of



Fig. 3. Left tummy tuck. Scar is barely visible. The incision is made with the right tummy tuck. The incision is made later, but is below the fold of the abdomen. The result is a more rounded abdomen.

voluminous gauze fluff or mechanical wadding. Large and a single light plaster hip spica with

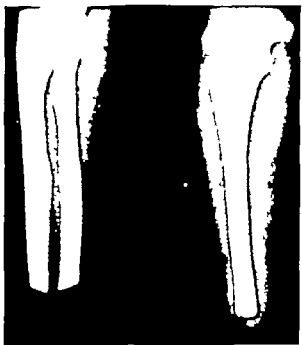


Fig. 4. The radius and ulna have been obliquely cut and rounded at the distal end of the forearm.

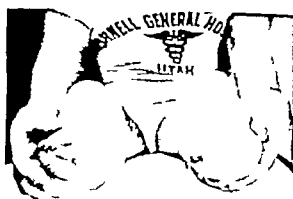


Fig. 5. Right tummy tuck. Scar is barely visible. The incision is made later, but is below the fold of the abdomen. The result is a more rounded abdomen.

the tummy in neutral position or in slight abduction and the dressing left in place 10 days. When dressing has been made under tension skin traction is applied with the kinetix over ace adhesive.

AMPUTATION OF THE FOREARM

If the guillotine amputation is to be near the wrist the site for amputation is selected where the muscular portion of the forearm tapers to form the distal tibia segment and wrist. An equal anterior and posterior skin flap is marked with methylene blue. At the angle over the radius, the skin is opened and a chisel mark is made in the radius to establish the site of amputation. This mark will be found very useful during the various stages in the amputation. Both skin flaps are cut and reflected and the distal skin is reflected as well to facilitate the fashioning of fascial flaps longer than the skin. The fascial flap is reflected only to the marked site of amputation. Nerves and vessels are identified, ligated and treated as described. The muscles are cut transversely at the site of amputation nothing is disturbed proximal to this point except the nerves. The periosteum of the radius and ulna is cut obliquely and stripped distally. With the two bones held parallel they are sawed obliquely about $\frac{1}{4}$ inch distal to the periosteum and the edges are filed (Fig. 4). The tourniquet is removed and all bleeding point are ligated. Overlapping of the fascial flaps under tension has proved beneficial because it affords better covering to the bone ends and does not

This is the procedure followed at the General Hospital and most not be interpreted as the standard for all Army amputation centers.

place the line of closure immediately under the line of skin closure thus giving freely movable skin over the stump end. The stump is lightly dressed, wrapped snugly to the elbow with two ace bandages and kept elevated. The ace bandages are loosened in 24 hours to relieve the pressure under which they were applied.

AMPUTATIONS ABOVE THE ELBOW

In revisions or reamputations of the upper arm as much length as possible is sought, the supracondylar amputation being ideal. Here maximum necessary skin may often be obtained by the use of skin traction a few days preceding surgery. Scar tissue of the guillotined end is removed by block and the bone end treated much the same as in thigh amputations. Equal skin flaps are dissected or such skin as is available to maintain length since the placing of the scar is not of prime importance on the nonweight bearing extremity except to avoid a scar on the anterior surface of the upper arm where slight pressure will be exerted in lifting the prosthesis. One point has come to our attention that is helpful in securing a good upper arm stump. It is customary to do the amputation with the arm abducted on an operating table. When the flaps are closed in the usual manner with the arm in this position it will be found later that with the arm held at the side there is a redundancy at the stump end. Therefore before closure of the fascial and skin flaps it is wise to place the arm first at the patient's side and then in abduction to the shoulder level to estimate properly the degree of tension at which to close. The same is true if a blood pressure cuff is used as a tourniquet. The cuff should be entirely removed, not just deflated, so that the tissues can assume their normal position before the tension of the flaps is estimated. The immediate postoperative dressing consists of

a light gauze fluff over the end followed by tight ace bandaging to be released and reapplied in 24 hours.

SUMMARY

1. Definitive amputation surgery of the lower leg, thigh, forearm, and arm at ideal levels has been discussed.

2. The period from which the stump first becomes dry to the definitive surgery is in proportion to the length of time the stump has drained and the virulence of the organisms that have been present.

3. A permanent stationary mark on the bone at the amputation site for reference during the operation materially aids in correct fashioning of skin, fascia, and muscle for closure.

4. To avoid posterior redundancy and insure a straight stump in below the knee amputations, the posterior muscles should be sectioned transversely at the site of amputation; the lateral muscles should be left in place from the amputated end of the fibula to the level of the tibial amputation and a wedge of gastrocnemius muscle should be removed at the medial and distal aspect of the tibia.

5. In thigh amputations a medial and lateral edge of muscle as well as tapering of the quadriceps femoris aids in preventing redundancy in obtaining a conical stump.

6. Beveling of the radius and ulna, imbricating the fascia and disturbing no muscular attachments proximal to the amputation site facilitate the fashioning of a better appearing and functional forearm stump.

7. The changing of the position of the arm from abduction to the neutral position at the patient's side before closure of fascia and skin will facilitate the correct estimation as to the tension at which to close the amputated end.

CONSERVATIVE MANAGEMENT OF ADOLESCENT SLIPPING OF THE CAPITAL FEMORAL EPIPHYSIS

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THE divergence of opinion on management of adolescent slipping of the capital femoral epiphysis in its various stages is evidence of limited success in the treatment of this condition. Many unsatisfactory functional results have followed currently popular methods of treatment.

This report is a review of 44 cases in which treatment was directed toward restoration of function. Trauma to the epiphysis by operation or manipulation was avoided when possible.

Recognition of early symptoms, signs, and roentgenographic findings has led to earlier diagnosis and treatment when epiphyseal displacement is minimal and no significant functional impairment present. Ossification of the epiphyseal cartilage growth disc in such cases is an accepted criterion of successful treatment if further displacement is to be prevented (9, 27, 31). Various surgical procedures have been advocated to hasten ossification of the growth disc or to fix the epiphysis to the femoral neck until bony union occurs (9, 14, 32). In the cases reported here closure of the epiphysis occurred within 3 to 12 months without additional trauma of drilling, etc. The longer disability occasioned by conservative treatment was of little economic significance in most instances. It is believed that the risk of damage to the blood supply to the epiphysis following operations outweighs the advantage of reducing the period of disability when nonoperative methods accomplish the same result over a slightly longer period.

With moderate displacement of the epiphysis, without bony union, discussion has centered chiefly on the indications for and against manipulative or operative methods of replacement. The question of the necessity or advisability of accurate replacement has not been settled. The general belief is that disabling arthritis is inevitable after the third decade if the deformity is allowed to persist and that accurate replacement of the epiphysis will prevent this late sequela. There is no evidence that the first contention is generally true, and reports in the literature show a high incidence of degenerative arthritis after several

years in patients in whom replacement by manipulation or operation has been done (4, 9).

Manipulative attempts at replacement of an epiphysis which has not yet united have failed in most instances (7, 9, 13, 15, 19, 22, 23, 25, 26, 27, 28, 30) to bring about any change in the anatomical relationship of the epiphysis with the neck unless the neck is fractured below the zone through which slipping takes place. The anatomical basis for this difficulty in replacing the epiphysis has been described by Wardle. Actually much depends on the rate of slipping. When acute displacement is present replacement is readily accomplished. The slower the rate, and the longer the displacement has existed the greater the difficulty of replacement. Correction of the limb deformity in long standing cases, without actual fracture of the neck, is usually at the expense of the capsule and ligamentum teres which may be badly torn. Many cases of progressive loss of motion and pain in the hip have been reported following this procedure (3, 4, 9, 15, 21, 22, 23, 24, 25, 31). Waldenström (27) and McMurray have reported aseptic necrosis of the epiphysis in 25 per cent of their patients so treated.

Gradual replacement by prolonged traction in adduction and internal rotation has been shown by Wardle to be successful in a number of cases. However Howarth reported 5 poor functional results in 7 patients treated by strong traction and immobilization. He reported good correction of the upward displacement of the neck in most of the cases, but found that the rotation usually could not be changed. Late irregularity of the shadow of the cortex of the head, irregular ossification of the epiphysis, and thinning of the articular cartilage on the roentgenogram were found in most of his cases.

Operative freeing of an epiphysis which has not united to the neck converts a slowly progressing displacement of the epiphysis into an acute fracture separation. The epiphysis is subjected to the danger of infarction unless the blood vessels in the ligamentum teres or undamaged posterior portion of the visceral capsule furnish adequate nutrition.

Rest has long been known to bring about considerable improvement of function if instituted

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Fig. Case 1. Hip joint. Note signs of epiphysis with cartilage. impending closure.

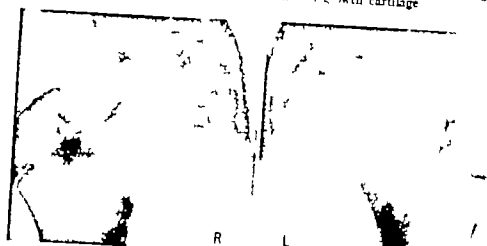


Fig. Case 2. Hip joint. Note signs of epiphysis with cartilage. impending closure.

during the stage of progressive displacement (8, 12, 15). Unless the anatomical deformity of the head and neck is severe a large component of the limb deformity and loss of function appears to be due to muscle spasm. Treatment by immobilization only was found to leave no significant functional impairment in over 47 per cent of the patients with moderate displacement of the epiphysis without union reported here. If the residual anatomical deformity of the epiphysis on the neck impairs abduction and rotation subtrochanteric osteotomy corrects the limb deformity without endangering the blood supply to the epiphysis.

If the epiphysis is united with the neck when the patient is first seen it is likewise obvious that reposition by force can only take place following fracture of the neck. In cases of this type surgical reposition can be brought about only by osteotomy of the neck. The coxa vara in such in-

stances has usually been of long standing and the postero-inferior portion of the capsule has become adapted to the changed position of the head. Thus tension on the capsule following reposition or injury to this structure when wedge osteotomy is done may occlude the vessels of the postero-inferior portion of the capsule.

End result studies 5 to 14 years after surgical reposition or femoral neck osteotomy have shown variable results in patients with moderate displacement with or without bony union. Wilson (30), Ghormley and Fairchild and Kleinberg and Bochman have reported good results in patients observed over this period. However a review of 87 cases recorded in the literature from 1924 to 1942 (3, 4, 7, 10, 11, 13, 16, 19, 21, 22, 29, 30) does not show encouraging results. Aseptic necrosis of the epiphysis is reported in 13 per cent of the cases following operation, and the reported poor results are over 50 per cent.

Soft parts contracture about the hip plays a significant rôle in preventing correction of the limb deformity after union of a severely displaced epiphysis has occurred. Anatomical replacement cannot be obtained without trauma to these structures. Such trauma predisposes to subsequent loss of motion and interference with the blood supply to the epiphysis. Correction of the limb deformity and realignment of the weight bearing surface of the epiphysis by extracapsular osteotomy has not led to these complications in such cases in this report.

Sudden trauma, superimposed on a slipping capital epiphysis, may result in complete separation. As in adults following fracture of the neck of the femur the blood supply to the epiphysis may be interrupted at the time of the accident or may be caused by additional trauma after the accident. It is believed advisable in such cases to avoid additional trauma by attempting to bring about reposition through gradual traction with the limb in abduction and internal rotation. This may be successful if separation has occurred within 4 to 6 weeks. After this period or if reposition by traction is impossible surgical reposition and internal fixation of the epiphysis seems indicated.

These facts and principles form the basis of the conservative treatment of 44 cases of slipped femoral epiphysis reported here. These cases have been observed at the University of Chicago Clinics during the past 14 years.

TREATMENT AND RESULTS

Bilateral displacement of the epiphysis was observed in 11 patients, or 25 per cent of the total number. The remaining 33 patients had involvement of one side only. A total of 55 displaced epiphyses were studied. Group I includes 29 hips in which epiphyseal displacement was minimal in group II are 23 hips in which displacement was moderate and in group III are 3 hips in which fracture separation of the epiphysis had occurred.

Good results are those with 90 degrees or more of flexion, 30 degrees or more of abduction, internal rotation of 5 to 10 degrees, and not more than 3 centimeters of shortening. Function is normal and painless with all activity. Fair results signify 45 to 90 degrees of flexion, 15 to 30 degrees of abduction, rotation to midposition only, and no pain with ordinary activity. Poor results are those with marked limitation of motion, deformity or epiphyseal necrosis. Intermittent pain is usual with ordinary activity. Uncertain results include cases followed elsewhere on which follow up studies were not available. Results are based on examination 2 to 6 years after treatment.

Group I minimal displacement. Minimal displacement was observed in 29 hips included in group I. Twenty-six of these were treated. Two of the remaining 3 showed osseous union when discovered and required no treatment. The third untreated patient showed roentgenographic evidence of union and aseptic necrosis of the epiphysis on admission. Treatment was directed toward alleviation of symptoms due to this complicating factor.

Two patients were treated by bed rest alone and closure of the epiphysis occurred without further displacement. This is not an approved method of treatment, however, as progressive displacement may take place under such circumstances. Treatment of the remaining 24 consisted of immobilization of the affected limb in plaster until ossification of the central portion of the epiphyseal growth plate took place. This required from 3 to 9 months. Wide abduction and internal rotation of the limb were considered important factors in removing the shearing stress from the epiphysis during this period. The plaster bandage encased the opposite thigh in abduction to prevent tilting of the pelvis and loss of abduction on the affected side. When bilateral displacement was present both limbs were immobilized in wide abduction and internal rotation. Spasm occasionally prevented attainment of this position. Bed rest for 7 to 10 days usually relieved this difficulty. No attempt was made to alter the position of the epiphysis on the neck.

The following case with minimal displacement exemplifies rapid ossification of the cartilage growth plate following a short period of immobilization alone.

CASE. C. C. boy, 5 years and 3 months of age, complained of pain on the inner aspect of the left thigh and knee of 3 months duration. Pain as present only when he was walking or running. Examination showed moderately obese boy with small external genitalia and prostate. Pubic and axillary hair was scant. There was centimeter of shortening and limitation of internal rotation of the left leg.

The roentgenogram (Fig. 1) shows slight upward displacement of the neck of the left femur on its epiphysis and the characteristic juxtaepiphyseal zone of osteoporosis. The right hip shows arrowing of the cartilage disc of the capital epiphysis. Sclerosis on both sides of the growth cartilage indicates imminent closure of this epiphysis.

Immobilization of the left leg in abduction and internal rotation for 6 weeks as carried out. Thus as followed by partial weight bearing with crutches for an additional 14 months. Four and one-half months after admission he was bearing full weight without support and ossification of the capital epiphyseal growth cartilage as complete (Fig. 2).

At this time closure of the opposite capital epiphysis as nearly complete. Examination 2 years later showed centimeter of shortening of the left leg, normal motion of the hip, and closure of the proximal femoral epiphyses of both sides.

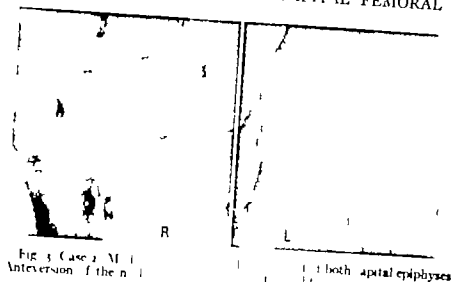


Fig 3 Case 2 Medial inversion of the neck

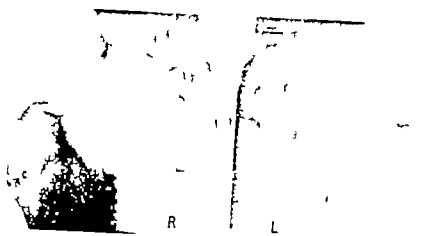


Fig 4 Case 2 Two and one half reduction of the displacement (Medial inversion) The hip is now painless

There has been no further displacement of the gait is normal and

The results in group I are summarized in Table I

TABLE I—RESULTS IN 29 CASES IN GROUP I

Treatment	Hips	Good	Fair	Poor	Uncertain
Bed rest					
Cast	1				
Traction and cast					
No treatment					(N)
Total treated	20	5			

(N) = Roentgenographic or pathologic evidence of aseptic necrosis of the epiphysis

Three of the patients in group I developed slipping while under ambulatory treatment for the same condition on the opposite side. All healed satisfactorily following immobilization. These 3 cases in which crutches or caliper brace were initially used are listed under treatment by cast since bilateral involvement necessitated immo-

bilization of the initially affected limbs which were not healed at the time slipping of the opposite epiphysis occurred.

The 1 poor result following treatment by traction and cast is noteworthy. The growth cartilage ossified as usual but severe atrophy and progressive loss of motion of the joint occurred. Temporary fibrous ankylosis was the outcome. Identical changes took place in the opposite hip in which epiphyseal displacement was slightly more marked. The cause of this phenomenon is unknown.

Arthroplasty of the hip was performed in the 1 case in group I with necrosis of the epiphysis. The pathologic findings in this case have been reported elsewhere (18).

Residual leg length inequality in cases of this group with unilateral involvement is determined by 2 factors: (1) by the amount of initial upward displacement of the femoral neck on its epiphysis and (2) by the amount of subsequent growth of

weight bearing surface of the epiphysis by subtrochanteric osteotomy.

The 3 cases in which bony union of the epiphysis was evident on admission showed density contrast between the epiphysis and the shaft and irregularity of the shadow of the epiphyseal cortex on the roentgenogram. In these cases with aseptic necrosis, improvement of gait, correction of deformity and partial correction of leg length inequality followed subtrochanteric osteotomy. Persistent intermittent pain with ordinary activity necessitates classification of these cases as poor results in spite of improvement which followed treatment.

Shortening of the affected side of 3 centimeters or less was not found to be of significance. Marked cervical-capital overrinding when present, is of as great importance as the growth arrest in the causation of leg shortening in this group. Another factor equally important in producing limb length inequality in cases with long standing disability is inhibition of growth of the epiphyseal cartilages of the tibia and distal end of the femur due to prolonged disuse of the limb. In 1 case showing evidence of bony union and epiphyseal necrosis on admission, displacement on the affected side, continued growth of the unaffected proximal femoral epiphysis, and retardation of growth of the lower femoral and tibial epiphyses on the affected side led to approximately 10 centimeters of shortening of the affected limb. Subtrochanteric osteotomy and a leg lengthening operation were necessary to correct this deformity.

Group III—complete separation of the epiphysis. Complete separation of the epiphysis following trauma was observed in 3 cases in group III. Sudden displacement occurred 2 weeks before admission in 1 case (Case 3). In a second case complete separation occurred following a fall 3 weeks before the patient was first seen, and the third case was referred 13 months after fracture separation of the epiphysis following injury.

Satisfactory reposition of the epiphysis was accomplished by gradual traction in the first case shown here.

CASE 3. E. S. boy, years and 0 months of age, was admitted weeks after fall resulting in pain, deformity, and shortening of the right leg. He had complained of mild pain in the right thigh and knee for months before the injury. Examination showed a thin, normally developed male. The right leg was shorter than the left and was externally rotated.

The roentgenogram (Fig. 5) shows complete separation of the right capital epiphysis. The right leg was held in abduction and internal rotation by adhesive skin traction for 16 days. A roentgenogram then showed marked but not complete replacement of the epiphysis. A plaster spica was then applied and was removed 3 1/4 months later when bony union was present (Fig. 6).

He was allowed full weight bearing months after the injury. Figure 7 shows the appearance 1 year and 6 months after admission, and examination 6 months later showed full range of flexion, extension, and abduction, with limitation of internal rotation to 1 degree.

The results in 3 cases in group III are summarized in Table III.

TABLE III.—RESULTS IN 3 CASES IN GROUP III

Treatment	Hips	Good	Fair	Poor
Traction and cast				(N)
Manipulation and cast				(N)
Total treated	3			

(N)—Roentgenographic or pathologic evidence of aseptic necrosis of the epiphysis.

In the second patient, admitted 3 weeks after complete separation of the epiphysis, satisfactory reposition was not obtained after traction over a 5 week period. Density contrast between the epiphysis and the atrophied bone of the shaft on the roentgenogram at this time indicated necrosis of the epiphysis, and replacement by open operation was considered advisable.

The third patient, first seen 13 months after complete separation of the epiphysis, showed roentgenographic evidence of necrosis of the epiphysis on admission. Reposition by manipulation under anesthesia elsewhere was followed by nonunion after immobilization in the Whitman position in plaster for 3 months. Excision of the epiphysis and arthrodesis of the hip were done. The pathologic findings in this case have been reported elsewhere (18).

A summary of the results following treatment in the 3 groups is seen in Table IV.

TABLE IV.—RESULTS IN 3 GROUPS

	Hips No	Good		Fair		Poor		Uncertain	
		No	Per cent	No	Per cent	No	Per cent	No	Per cent
Group I	26	23	88.5				5		
Group II	23		47.8	3				4	17.5
Group III	3		23				60.6		
Total	52	23	67.3	3	5.8		54.4	4	7.7

COMPLICATIONS AND SEQUELAE

No permanent limitation of motion of the knee was encountered following immobilization over periods up to 9 months. Knee function returned to normal after 2 to 4 months.

Genu valgum following stretching of the medial collateral ligament and capsule of the knee was an

occasional problem. This complication occurred in limbs subjected to prolonged heavy skin traction. Relief of spasm by general anesthesia seems advisable if not accomplished by skin traction after 8 to 10 days. Prolonged traction when indicated is maintained better by means of a threaded wire inserted through the distal metaphysis of the femur.

Progressive loss of motion and fibrous ankylosis of the hips occurred in 1 patient with bilateral involvement. Displacement was minimal on one side and moderate on the other. The result 4 years later was marked limitation of motion and advanced degenerative arthritis of both hip joints. Explanation of this unusual sequela is difficult. The articular cartilage became thinned and the shadow of the epiphyseal cortex on the roentgenogram became irregular, but both epiphyses underwent marked disuse atrophy comparable to that of the shafts which spoke against necrosis of the epiphyses. The marked stiffening of the joints with identical changes on both sides suggests a severe nonspecific inflammatory reaction as the cause of these changes.

Aseptic necrosis of the epiphysis was observed in 1 instance out of 29 patients with minimal displacement. Of 23 moderately displaced epiphyses in group II aseptic necrosis was observed in 4. Of these, 3 showed evidence of necrosis of the epiphysis on admission and in 1 case necrosis followed progressive displacement of the epiphysis in a limb inadequately protected by a nonweight bearing caliper brace. Necrosis occurred in 2 of the 3 epiphyses in group III following complete separation.

Infarction of the epiphysis in adolescent epiphysiolysis may be followed by early degenerative changes in the hip joint. Such changes lead to considerable disability. Knowledge of the pathologic changes in a joint with this sequela has been scanty. Necrosis of the epiphysis, after surgical reposition is accepted as inevitable by some authors (16). They as well as others, advocate prolonged protection of the epiphysis from weight bearing to prevent collapse of the head during the period of replacement of the necrotic bone. If the overlying articular cartilage remains alive, and no collapse takes place, good function might be expected. Such circumstances may explain the good results observed by these authors.

In adults Axhausen and Bergmann (2) and Phemister have shown that articular cartilage overlying areas of bone infarction frequently becomes necrotic. Phemister has shown that necrotic cartilage undergoes replacement by fibrocartilage or in part by bone. Axhausen (1)

showed experimentally and clinically that degenerative arthritis was a common sequel to necrosis of the cartilage on one side of a joint.

In a previous description (18) of the pathologic changes in the epiphysis of 2 cases included in the present report it was shown that in adolescence complete or partial necrosis of the articular cartilage may occur after infarction of an epiphysis. The articular cartilage in these cases was undergoing replacement by fibrocartilage and bone.

Preservation of the circulation to the epiphysis is therefore of importance if degenerative arthritis and poor joint function are to be avoided. Clinical observations of others support this contention (4, 25).

SUMMARY AND CONCLUSIONS

1. The methods employed and the results in the treatment of 44 cases of adolescent epiphysiolysis in various stages of displacement are reported. Reposition of the epiphysis was not usually attempted and was not accomplished in any case except in those in which there was recent complete separation of the epiphysis following sudden trauma.

2. Of 26 hips with minimal displacement of the epiphysis treated in group I good function was obtained in 88.5 per cent following immobilization and protection of the affected hip until ossification of the capital epiphyseal growth cartilage took place.

3. Good function was obtained in 47.8 per cent of 23 hips with moderate displacement of the epiphysis in group II following the conservative plan of treatment outlined. Thirteen per cent resulted in fair function and 21.7 per cent had poor results. In only 1 case or 4.4 per cent of the total could the poor result be attributed to treatment. Results in the remaining 17.5 per cent of the cases are not known.

4. Satisfactory replacement of a living epiphysis and a normally functioning hip followed prolonged adhesive skin traction and immobilization in 1 or 33.3 per cent, of 3 cases in group III with complete separation. In 2 cases, poor results were due to necrosis of the epiphysis.

5. Epiphyseal necrosis may occur naturally in cases with minimal displacement. It is not uncommonly present in cases with moderate displacement first seen after bony union of the epiphysis has occurred. It is frequent following complete separation of the epiphysis due to sudden trauma.

6. Death of the epiphysis, as a complication following manipulative or surgical reposition of the epiphysis, is reported in a relatively high per

I commend to your earnest attention the enclosed editorial by Dr Loyal Davis copied from *SURGERY GYNECOLOGY AND OBSTETRICS*, one of the leading influential medical journals of this country. The point of view expressed by Dr Davis is I know, shared by many members of the U S Army Medical Corps and by civilian physicians.

On October 30 Senator Tydings replied as follows

I am in the office today for about an hour after an absence of some two weeks because of speaking engagements throughout the State in connection with my campaign. I found your letter of the 23rd awaiting me, with the editorial by Dr Loyal Davis concerning the Army Medical Corps.

Time does not permit me to read the article as carefully as I should like it at the moment, for I have two or three radio talks I must write together with an accumulation of senatorial and political correspondence requiring my personal attention.

"I feel, however that I have grasped the point made by him and I think it worthy of further examination. In the meantime I am forwarding Dr Davis article on to the Secretary of War believing that the points raised by Dr Davis are worthy to be considered in order to give the greatest amount of efficiency to the Army Medical Corps.

I hope something constructive may come out of this endeavor and I appreciate your letting me have the editorial by Dr Davis.

And a few days later he courteously forwarded the following letter to himself from the Secretary of War

"Thank you for sending me a copy of the editorial by Doctor Loyal Davis which I have noted and am returning in accordance with your request.

As you know we are constantly studying the efficiency of the administrative and operational aspects of the War Department with an aim to achieving greater efficiency. The problem raised concerning the Surgeon General and the medical mission is constantly under review and I know that the point of view raised in the editorial will be carefully considered in trying to achieve greater economy in the use of Medical Department personnel and facilities.

Senator Radcliffe sent two letters in reply as follows

I have been reading with very much interest, indeed, your letter of October 3 enclosing a copy of an editorial entitled 'Organization of the Red Army Medical Corps' by Dr Loyal Davis.

"Since I am a layman, my views probably should not be very definite but it seems to me that there is

very much force in what you write me and in what Dr Davis says in his editorial.

All this brings back to my mind various discussions which I heard during and shortly after the first world war. You will recall of course Dr Welch, Dr Young, Dr Baer, Dr Stone, and many other of the outstanding physicians and surgeons of the Johns Hopkins Medical School took a very active part in the war and rendered invaluable service. I remember that several people stated that the situation was very anomalous when a man like Dr William Welch, so prominent in medicine as any one in the world, should occupy a subordinate rôle, not in military medicine administration merely but in other matters more technical. Rearrangements were made which eliminated most of the objections.

I am very glad you wrote this letter to me and I am using it as a basis of some inquiries and discussion about the matter.

I received today a letter from Judge Patterson in regard to the article on 'Organization of the Red Army Medical Corps'. He and Secretary Stimson are discussing this matter.

General Marshall referred the covering letter and Dr Davis editorial to the Surgeon General who on November 6 replied as follows

Your letter and the inclosure of the editorial from *SURGERY GYNECOLOGY AND OBSTETRICS* by Dr Loyal Davis has been forwarded to me by General Marshall with the request that I acknowledge it. I expressed my evaluation of the editorial by pointing out that in my opinion the editorial probably expressed the feelings of the overwhelming majority of the 45,000 Medical Corps officers in the Army Medical Corps. In addition I pointed out that the subject is of sufficient moment to warrant study since it is essential that all steps be explored which could possibly contribute to the more efficient utilization of Medical Department personnel and facilities.

"Thank you for your interest in calling this editorial and the problem which it raises to the attention of General Marshall.

There can be little doubt in the minds of doctors in or out of the military service that the present organization of the Medical Corps of the United States Army is wholly unsatisfactory and should be changed. The marvel is that the Medical Corps, handicapped as it is by faulty organization, hampered as it is by medically uninstructed line officers, has accomplished so much. It could do much more. It is to be devoutly hoped that the ripple created by Dr Davis' stone tossed into muddy

waters will become a tidal wave leading to critical study review and rapid change of a medically intolerable situation

JOSEPH EARLE MOORE

PLASMA

EXPERIENCE in the Mediterranean (North African) Theater of Operations embracing campaigns in Tunisia Sicily, Italy and France has afforded ample opportunity to evaluate the usage of plasma infusion in wounded and injured men. It was anticipated immediately observed and has been subsequently confirmed that plasma is not a physiologic substitute for whole blood in the management of the seriously wounded and injured. Plasma can be considered a substitute only in so far as it can be shipped stored and made available in the combat zone where refrigeration laboratory testing and other safeguards that must surround blood transfusion cannot be provided. Even here it is a substitute only for the purpose of restoring or maintaining blood volume during the period of delay necessary to transportation and the starting of a whole blood transfusion.

The recovery from shock that follows plasma infusion affords a false sense of security to the doctor who administers it—particularly if he is not an experienced surgeon. It may encourage him to attempt operative surgery that the patient is not prepared to withstand. Restoration of blood pressure and volume flow before hemorrhage has ceased or under conditions in which it cannot be arrested immediately by surgical operation leads to further loss of red cells and terminates in disaster. When surgery must be delayed it may be essential to keep the patient alive with plasma, but not to attempt to establish full

circulatory compensation. A systolic blood pressure of about 85 millimeters has been designated as a safe compromise level. On reaching hospital where surgery is to be performed blood and blood plasma are used in relative amounts of about three and one.

Plasma is looked upon as a first aid measure for dire surgical emergencies not as a safe or satisfactory therapeutic agent for hemorrhage. It is a supplement not a substitute for whole blood. Specific indications for its usage are found in the management of burns and a few other conditions in which only the plasma is lost from the circulation. Even in these instances it appears that objections to the employment of whole blood have been exaggerated.

In the United States a wide and sustained publicity campaign has been required to secure blood from voluntary donors for conversion into dried plasma to meet the requirements of the Army and Navy. Large overhead investments have been made in processing plants. This effort cannot be commended too highly; the needs have been met and thousands of lives saved.

However a solemn word of warning is not amiss at this time. An attempt to project the use of plasma into the emergencies of civilian surgery as a substitute for whole blood except as here defined will exact a high price in human life. *This has happened many times under circumstances beyond control because of the exigencies of war.* It will also increase the cost of surgical care to an extraordinary degree by the unnecessary use of an innocuous but expensive and fashionable method of therapy. The vitamin racket can be made to appear a pale and small time affair in contrast.

EDWARD D. CHURCHILL,
Colonel MC A US

AMERICAN COLLEGE OF SURGEONS

1945 WAR SESSIONS DEFERRED

THE American College of Surgeons, as an aid to the war effort has deferred its 1945 series of War Sessions at the request of the War Committee on Conventions of the Office of Defense Transportation for the curtailment of meetings until such time as the present emergency has passed and conditions have improved.

Plans had been completed for the February meetings in St. Louis, Louisville, Milwaukee and Cleveland because earlier indications were that sessions of a strictly educational nature limited to relatively small local areas, and bearing upon military and civilian health, would be sanctioned by the committee. However in a special communication which has been received by Dr Malcolm T MacEachern, asso-

ciate director of the College, the secretary of the committee Mr R. H. Clare wrote in part as follows

"This Committee has reviewed your application and has decided that these War Sessions can reasonably be deferred because of the present critical transportation and housing situation. While we appreciate the contribution already made by the American College of Surgeons in discontinuing all national meetings, it is necessary to request this further curtailment of your activities at least until such time as we have passed the present emergency and conditions have improved. We will need your complete co-operation if the objectives of this Committee are to be attained and we are confident that we will receive your support."

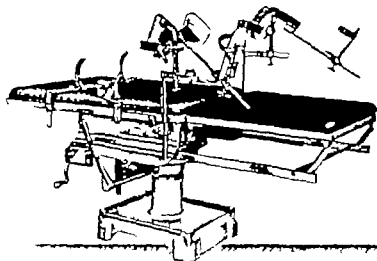
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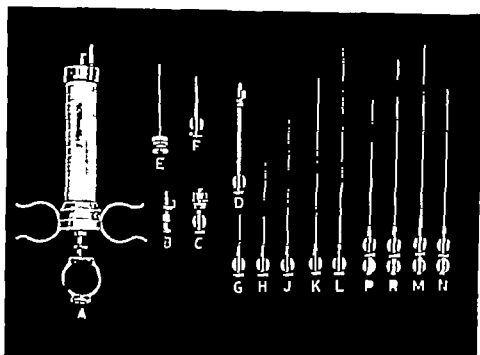
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SURGERY

GYNECOLOGY AND OBSTETRICS

An International Magazine, Published Monthly

VOLUME 80

APRIL, 1945

NUMBER 4

CALCIFICATION OF THE TENDON CUFF OF THE SHOULDER

M BECKETT HOWORTH M.D. Sc.D (Med.) F.A.C.S. New York, New York

CODMAN and others have demonstrated that the condition called subdeltoid bursitis or periarthritis is in reality a lesion of the tendon cuff of the shoulder. It may be a calcification or a tendonitis. Calcification of the tendon cuff is probably the most common cause of pain and disability at this joint. Codman deserves great credit for his contributions to our knowledge of these shoulder lesions especially his demonstration of the relationships between bursa and tendons and between the clinical and pathological features and the operative treatment. He has shown that the primary lesion is in the tendon and that the bursitis is secondary. The present discussion is limited to calcified tendons.

Javjavy in 1867 and Gruber in 1869 described the pathology of subdeltoid bursitis. Duplay (12-15) in 1872 and 1896 without benefit of roentgenography described periarthritis of the shoulder probably including in this vague term cases of calcification. Kuester in 1902 reported additional cases. Harrington and Codman (7) did the first operation upon a shoulder with calcification in the tendon cuff in 1902 but did not recognize its true nature and considered it an abscess. Painter and Codman (7) operated upon a second patient in 1905 and then recognized the true

nature of the lesion and the relation between the clinical and the pathologic picture. Baer in 1907 and Bergemann and Stieda in 1908 also advised operation for this condition and the latter further described the pathology. Moschowitz in 1915 and Codman and Aker son (11) in 1931 described the pathology of their cases. Numerous authors have reported cases and the results of treatment by physical and roentgen therapy. Aspiration of the bursa was reported by Flint in 1913, multiple puncture of the calcified area of the tendon by Milgram.

ANATOMY

The tendons of the subscapularis, supraspinatus, infraspinatus and teres minor muscles converge and fuse with the capsule of the shoulder joint about 1 inch from its distal margin. The common tendon-capsule cuff thus formed is attached to the superior margin of the tuberosities and the anatomic neck of the humerus. The subdeltoid or subacromial bursa lies upon this tendon cuff and the greater tuberosity and is covered by the deltoid muscle, acromion process and coracoacromial ligament. It is a thin walled transparent hemispherical pouch averaging about 1½ inches in diameter and lined with synovial membrane. The floor of the bursa is attached to and moves with the cuff and great

From the New York Orthopaedic Dispensary and Hospital.

er tuberosity and the roof moves with the structures covering it by means of the redundant folds at its margin. The tendon cuff is normally seen shining through the superior half of the bursal floor. The intertubercular groove and biceps tendon are seen and felt near its medial portion.

PATHOLOGY

The bursa and the calcareous deposit were exposed at operation in 23 shoulders. The bursal wall was usually thickened and opaque, edematous and vascular. Only one bursa contained calcareous material in a thin suspension. Small villi were present opposite the tendon lesion in several cases. The membrane in the more chronic lesions was firmer and white.

The calcareous deposit could be identified in the floor of the bursa as a white or yellowish area, often a raised mound resembling a boil surrounded by a reddish zone. The white area was softer and more elastic than normal tendon but sometimes quite tense. Upon incision the contents might be a milk like liquid and spurt forth under pressure, creamy or cheese-like and ooze forth like tooth paste from a tube or dry and amorphous, granular or sand like, having to be dug out with knife point or curette. The number of cavities varied from one to five, their lengths from $\frac{1}{4}$ to $1\frac{1}{2}$ inches, their contents from 0.5 to 4 cubic centimeters. When there were two or more cavities the contents might vary in the different cavities. Usually the cavities were separate and distinct but some of them communicated or had peripheral burrows. Some of the cavities were smooth walled but not encapsulated, others were irregular and vaguely outlined. The cavities lay in tendon, the fibers of which were softened, stringy and dull. The degenerated tendon often was infiltrated with calcareous granules or clumps. Bare bone was exposed in the base of some of the cavities. No communication with the joint was demonstrated, and only one had ruptured into the bursa. No frank tear of the tendon was seen. Most of the deposits were in the tendon of the supraspinatus but there were several in the infraspinatus and the teres minor, one in the subscapularis muscle.

Microscopic sections from the tendons demonstrated degenerated and frayed ligaments, fibrous and fibrocartilaginous connective tissue. The degenerated areas contained calcium salt deposits in the form of conglomerate and scattered fine and coarse granules and scattered amorphous nodules, the deposits being most extensive in the areas of greatest degeneration. Foreign body giant cells were sometimes present. Evidence of repair was often manifested by the picture of connective tissue proliferation and an associated abundance of blood capillaries. The synovial membrane of the adjacent bursa was edematous, hyperemic, thickened and exhibited hyperplasia of synovial cells, sometimes with villous formation.

ETIOLOGY

The cause of the calcification was not obvious, but it appeared that there had been first a degeneration of the tendon followed by the deposition of calcium salts. The degeneration may be the result of impaired circulation, attrition or both. The supraspinatus tendon with the arm at the side makes a curve of about 40 degrees around the head of the humerus to its insertion. This is the common working position of the arm and the abduction of the arm in this position, especially with sudden or resisted movements, causes considerable pressure against the tendon. Any irregularity beneath the tendon increases this pressure and wear. There is a similar situation for example where the short extensor and abductor of the thumb cross the radial styloid producing a tenosynovitis (de Quervain's disease). Motion picture film may be badly scratched in a similar way when it is wound jerkily on a reel. Similar effects may be produced in the tendons of the shoulder rotators by similar rotary motions. Constantly repeated motions seem more likely to produce this effect than varied and intermittent ones. The occupational history of the patients in this series, and the manner in which they have used their arms, tends to confirm this theory of the mechanism of the cause of this condition. Thus the use of the arm at the side with sudden jerky or resisted motions toward abduction or rotation constantly repeated, ap-

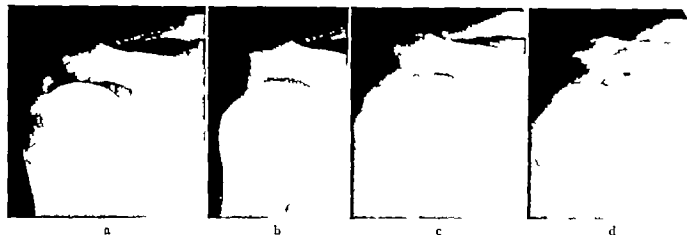


Fig. 1. Roentgenograms showing moderate calcareous deposits in supraspinatus tendon, plainly visible in all views. Pain which was present for 2 days improved

spontaneously. a Anteroposterior view b internal rotation 45 degrees c external rotation 45 degrees d external rotation 90 degrees

appears to be the cause of degeneration and calcification of the tendons of the shoulder cuff

COURSE AND STAGES

The symptoms and signs of this disease are not proportional to the size shape number and location of the calcareous deposits nor even to their type. Large deposits may be almost symptomless small deposits may be associated with considerable pain. Similar symptoms and signs may be present in the absence of deposits. Mild symptoms may suddenly become severe or severe symptoms subside with no change in the roentgenogram. It is probable that the most important factor in relation to the severity of symptoms and signs is the tension of the calcareous material in the substance of the tendon.

The calcareous deposits often increase occasionally decrease in size and density over a

period of months or years but may change in a few days. Rupture of the deposit into the bursa results in a change in the location and density of the calcareous material and is usually followed by immediate relief of symptoms and absorption of the material. Occasionally the deposits in the tendons are absorbed but most of them persist for many years unless there is a spontaneous or surgical opening.

The disease may be described as being in an acute chronic or quiescent stage but there is little relationship between the stage of the disease so expressed and its duration as one of long duration may suddenly become acute while one of short duration may be and remain clinically quiescent.

Thus it is seen that there is usually little correlation between the clinical and roentgenographic features of the disease.



Fig. 2. Roentgenograms revealing large multiple calcareous deposits in supraspinatus tendon, showing well in anteroposterior and internal rotation views, partly hidden by greater tuberosity in external rotation views. Pain which

was present for 1 week was relieved in 4 weeks with roentgen therapy. a, Anteroposterior view b, internal rotation 45 degrees c, external rotation 45 degrees d, external rotation 90 degrees.

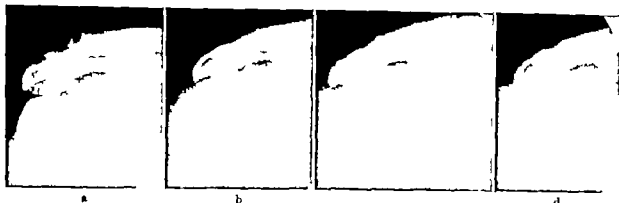


Fig. 3. Roentgenograms revealing moderate calcareous deposits in supraspinatus tendon, plainly visible in all views. Pain which was present for months became worse

with diathermy. a, Anteroposterior view b, internal rotation 45 degrees c, external rotation 45 degrees d, external rotation 90 degrees

THE CASES

One hundred consecutive cases have been included in this series. The average age was 43 years the range from 24 to 63. Only 1 patient was under 30 years, 12 past 50 years. Forty per cent were men, 60 per cent women. The right shoulder was affected in 62 per cent, the left in 38 per cent, 14 per cent being bilateral. Definite injury was mentioned in only 3 cases. Housekeeping was the most common occupation, while stenography, filing and similar activities requiring repeated sudden movements of the shoulders were done by most of the other patients. There was no evidence that focal or other infection had any relation to the disease.

SYMPTOMS AND SIGNS

The symptoms were pain, limitation of motion and disability. They varied in severity from slight to severe. The duration of symptoms was 2 days to 20 years, averaging 2 years. Only 24 had symptoms of less than 1 month's

duration, nearly all of the others came in because of exacerbations.

The pain was usually described as an ache in the anterior shoulder region, often radiating down the anterior border of the deltoid to its insertion. The pain overflowed into the forearm and upper shoulder girdle region in the more severe cases. It was worse at night, making it difficult to find a comfortable position in bed, especially on the affected side. The pain was worse on activity and often affected by weather. Abduction or putting the hand behind the head was difficult or impossible. Disability varied in proportion to the amount of pain and the use to which the arm was put.

The arm was usually held at the side in internal rotation. There was atrophy of the deltoid and spinatus muscles. Tenderness of various degrees was found usually anterolaterally just above the greater tuberosity because of the more frequent involvement of the supraspinatus muscle. The tenderness was lateral to the tuberosity with involvement of



Fig. 4. Moderate calcifications in supraspinatus and subacromioclavicular tendons, former showing well in anteroposterior and internal rotation views, latter in external rotation.

tion. Pain for months worse with diathermy. a, Anteroposterior view; b, internal rotation 45 degrees, c, external rotation 45 degrees, d, external rotation 90 degrees.

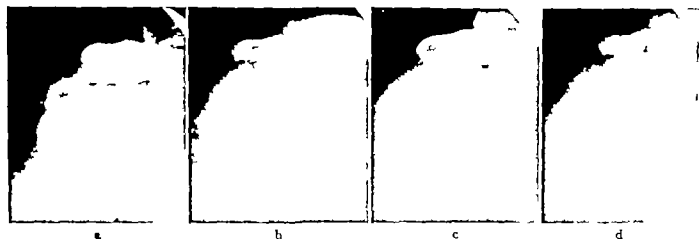


Fig 5. Large, multiple calcareous deposits in supraspinatus tendon, showing well in anteroposterior and internal rotation views, displaced medially in external rota-

tion views. Pain of 2 years' duration a, Anteroposterior view b internal rotation 45 degrees c, external rotation 45 degrees d, external rotation 90 degrees

the infraspinatus posteriorly for the teres minor and anteromedially for the subscapularis. Abduction was usually painful especially at the point where the bursa slides under the acromion. Painful rotation particularly externally was indicative of inflammation of the bursa. *Resisted motions* were painful: external rotation for involvement of the infraspinatus and teres minor; internal rotation for the subscapularis; abduction for the supraspinatus. Active or resisted motion was more painful than passive motion because of the increased tension on the diseased area and the increased pressure of the deltoid muscle.

Tears of the tendons of the shoulder cuff are distinguished by their sudden onset with injury, swelling at the tuberosity, a tender depression above the tuberosity, inability to abduct the arm, and difficulty in maintaining it in abduction whereas rotation is only slightly affected. There is the disturbance of scapulohumeral rhythm and the jog wince and crepitus described by Codman as the torn edge passes under and out from the acromion.

Tendonitis (frozen shoulder) is characterized by considerable limitation of all motion with pain and spasm and diffuse tenderness. The tendon of the long head of the biceps may be adherent to the groove in such shoulders.

LABORATORY

Routine urine examinations, blood counts and erythrocyte sedimentation rates were nor-

mal in all cases and cultures of the contents of the cavities resulted in no growths.

ROENTGENOGRAMS

The typical roentgenogram revealed an amorphous calcification in the angle between the humeral head, greater tuberosity and acromion. However, there was considerable variation in the number, size, shape, density, homogeneity, continuity and location of the calcifications. Usually there was one main mass, once as many as five. The mass generally was roughly elliptical, measuring from $1\frac{1}{2}$ by $\frac{3}{4}$ to $\frac{3}{8}$ by $\frac{1}{16}$ inches. It might be continuous or broken, of even or variable density, rounded or angular, sharp and smooth edged or irregular and fading. The smooth edged mass of even density but faintly flocculent under magnification of two or three diameters was usually liquid, whereas the broken ones of uneven density proved to be infiltrating and gritty. The supraspinatus calcifications were located just above the junction of the greater tuberosity and head, whereas those of the infraspinatus and teres minor were lower and superimposed upon the tuberosity except in internal rotation, that of the subscapularis was superimposed on the joint in internal rotation, on the head in external rotation.

The bursal calcium shadow extends down over the tuberosity and is apt to be faint and homogeneous.

The roentgenogram should be made tangential to the acromiohumeral interval and

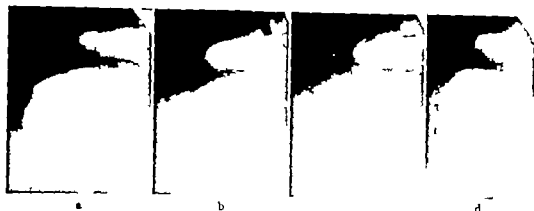


Fig. 6 Roentgenograms showing moderate calcifications in infraspinatus tendons, visible only in internal rotation. Pain for 5 months. Improved spontaneously over 8

months period. a, Anteroposterior view; b, internal rotation 45 degrees; c, external rotation 45 degrees; d, external rotation 90 degrees.

views should be made in 45 degrees internal and 45 and 90 degrees external rotation as well as in the neutral position. The single view even stereoscopic may fail to show one or more of the calcifications. Fluoroscopy may be of considerable aid in locating the deposits.

TREATMENT

Analysis of the effect of treatment in the hundred cases reveals

Pain and spasm may be relieved in some cases, especially the acute ones of short duration by any one of several treatments. Rupture of the calcareous deposit into the bursa spontaneously or by any form of treatment gives immediate relief. Rest alone may give some comfort. Additional relief may be obtained by immobilization or suspension in a comfortable position. However immobilization tends to produce stiffness and should be used only for a short time if at all and then combined with exercises as below. Immobilization is usually accomplished with the arm at the side in internal rotation causing contracture resulting in limited abduction and external rotation. This tendency is aggravated by the facts that the arm normally rests at the side and that external rotation is the least common motion and is normally less than internal rotation.

Heat in the form of a lamp, hot water bag, electric pad or hot packs, may provide some relief. Short or long wave diathermy may relieve some shoulders, and may even be fol-

lowed by absorption of the calcareous material in the early acute ones. However an acute shoulder with inflammation of the bursa, or tension in the tendon is often made worse by heat.

Cold is usually more comforting than heat especially in the very acute cases. Ice packs may be used but the ethyl chloride spray as reported by Kraus, is usually more effective. The painful areas are sprayed intermittently for several minutes (30 to 50 c.c.) but without actual freezing and pendulum exercises are begun immediately. The local anesthetic effect causes the muscle spasm to relax permitting the exercises, which are the most important part of the treatment.

Massage of the bursal region is likely to increase the pain in most cases though gentle massage of the adjacent muscles may be used to maintain muscle tone. Manipulation or stretching usually increases pain and spasm and often does more harm than good. Stretching under anesthesia is particularly apt to be disastrous as the inflamed or degenerated tissues are fragile and easily injured and it is these tissues rather than adhesions that are torn. Relief is sometimes obtained with manipulation however by rupture of the cavity.

Exercises are of great value and are the most important of the various physical therapeutic measures. They may be used independently at certain stages or in conjunction with the spray, irrigation, puncture, or operation. Exercises should be active rather than



Fig 7



Fig 8



Fig 9

Fig 7 Large calcification in infraspinatus tendon seen well in lateral view of humerus with arm abducted. A good view for this tendon, and for the subscapularis. Pain for 4 days, following lifting. Operation released thick milky fluid with calcareous granules in bulging tendon. Tendon degenerated. Relieved.

Fig 8 Large calcification in subscapularis tendon (superimposed on femoral head) as seen in external rotation. Pain for 1 year. No relief with diathermy. Operati n

Several hard white nodules in tendon with soap-like material under pressure. Three communicating cavities. Result excellent for 2 years.

Fig 9 Large single calcareous deposit in supraspinatus tendon. Pain for 4 years. Worse after diathermy and after irrigation. At operatio cubic centimeters of milky fluid under tension was released. Granules infiltrated the degenerated tendon. Result for a period of 3 years was excellent.

passive although the arm may be supported at times to reduce the effect of gravity. They should be done slowly and gently within pain limits in the most favorable positions. They should be graduated first with assistance then against gravity and finally against resistance.

The pendulum exercises are the simplest easiest, and least painful; they should be done with the arm in flexion and hanging loosely, i.e. with the trunk flexed or with the subject lying prone upon a table with the arm over the side. The arm is swung gently from the shoulder back and forth and from side to side and in a circle and rotated. Next, the arm may be rotated with the subject in the supine position and abducted preferably on a polished surface. The wall-crawling exercise in flexion and in abduction may follow. Assistance may be gained by using a light bar rope and pulley or the spokes of a large wheel mounted vertically. Similar exercises may be performed under water with the buoyancy of the water for support.

Radiotherapy sometimes relieves the acute attacks but has little effect on the chronic ones. Absorption of calcium salts may follow in the early acute cases but usually does not occur in the chronic type. Repeated or inten-

sive roentgen radiation is undesirable as it may increase the degeneration of the diseased tissues or burn the skin.

Novocain injection gives temporary relief which may be prolonged by the drainage through the needle punctures. Novocain iontophoresis is reported¹ to give relief in some cases.

Aspiration irrigation or puncture of the calcified area may give relief chiefly by the release of tension. It is necessary for success that the needle enter the cavity that it be large enough and the contents liquid enough to flow through the needle. Aspiration or irrigation of the bursa is helpful only if there is fluid in the bursa which is rarely the case. The needles must usually enter the cavity in the tendon in order to have any effect even when the contents are liquid. Improvement occurs by drainage of the liquid to the outside or into the bursa, where it is absorbed. The cavity can usually be entered by accurately locating the tender spot. Fluoroscopic control may be more precise but aseptic technique cannot so easily be maintained and there is danger of roentgen burns of the operator's hands on repeated exposure. It is desirable to wash as much of the calcified mate-

¹Personal communication, Kruse and Soow.

nal out of the tendon as possible. Failure is due to using a needle that is too small missing the cavity or the contents being too dry and firm. Successful aspiration irrigation or puncture is simple safe and effective not only in relieving pain but also in removing the calcareous material and the results immediate and late are good.

OPERATION

Operative drainage of the calcified cavity in the tendon offers the surest and most permanent relief of any type of treatment, and is often the best or only method of removing the calcareous deposit. Consequently immediate relief of pain and spasm and permanent healing of the lesion are obtained with operative treatment in a higher proportion of cases than with any other treatment.

A short incision is made anteriorly below the acromion and the fibers of the deltoid muscle split near its medial border thus exposing the bursa. The bursa is opened and inspected. The soft white areas with surrounding erythema in the floor of the bursa, locate the lesions. The whole floor may be inspected by rotating the arm and retracting the wound in various directions. Each area is incised in line with the fibers of the tendon thus releasing any liquid which may be present. The more solid portions are lifted out with a curette or dug out with the point of the scalpel. The loose or degenerated strands are excised. The defect is sutured in so much as this will bring the edges closer together. The bursal incision may be loosely approximated like wise the deltoid muscle.

POSTOPERATIVE CARE

A sling and swathe are used at night if necessary for protection. The arm was suspended in slight abduction and neutral rotation in some cases but this is not necessary. Exercises are begun the day after operation at which time the motion is often better than before operation. Exercises are progressive according to the amount of pain and spasm. Ethyl chloride spray may be used for relaxation in the occasional case with considerable pain and spasm after operation. The sutures are removed in 5 to 7 days, and underwater

exercises may be begun as soon as the wound is healed. The infra red lamp and gentle massage may be used as indicated.

There is usually immediate relief of the pre-operative pain especially in the acute and severe cases. Pain due to the incision is usually slight and subsides in 2 or 3 days. Motion returns to normal in a week or two in the cases with liquid material without infiltration. Motion improves more gradually in the shoulders with multiple or gritty infiltrating calcifications requiring 2 months or sometimes longer for return to normal.

RESULTS

We have operated upon 23 shoulders (22 patients) with calcification of the tendon cuff at the shoulder in the past 6 years. Eighteen were followed from 3 months to 6 years an average of 19 months. Most of these shoulders had previously been treated with physical or radio therapy without relief. Those with no pain weakness disability or limitation of motion were considered excellent results. Those considerably improved, but with slight or occasional symptoms were considered good results.

There was immediate and continued relief of pain and improvement in motion and use of the shoulder in all cases. The result of the followed cases was excellent in 5 good in 10 and fair in 3. The contents of the cavity were liquid in 4 of the excellent result shoulders whereas they were dry and gritty in most of the good results and 2 of the fair ones. The other fair result had a manipulation of the shoulder just before the operation at which adhesions were torn.

The excellent results in the liquid content shoulders were better and more quickly obtained than in similar cases in which patients were treated by puncture or irrigation 2 being failures after treatment by irrigation. The results for the shoulders with dry or infiltrating lesions were much better than the results in similar cases in which patients were treated by irrigation or puncture, physical therapy or radiotherapy. One had been treated by irrigation 10 by diathermy and 2 by radiotherapy without improvement and some had become worse. Five of the tendons with liquid

contents had been treated with diathermy with radiotherapy, without relief

Thus the improvement with operation was usually obtained more quickly and more surely while the eventual result was often better than with any other form of treatment

PROPHYLAXIS

It appears that degeneration and calcification in the tendon cuff of the shoulder is due to attrition and circulatory damage *The use of the arm at the side a sequence of the evolution and civilization of man has produced a mechanical disadvantage and increased the wear on the tendon cuff* The lesion might be prevented or reduced in severity by avoidance of the use of the arm in this position especially for jerky forceful tense or resisted motions in abduction or external rotation Correction of the position and manner of use of the arm and the posture of those persons with contributory occupations should largely prevent the lesion Warming up the muscles before use and keeping them in good physical condition by regular moderate exercise also should aid in the avoidance of this condition

SUMMARY AND CONCLUSIONS

The symptoms signs roentgenographic appearances and etiologic factors in one hundred cases of calcareous degeneration in the tendon cuff of the shoulder are reviewed. The pathology of the 23 shoulders operated upon is described The results of treatment by physical therapy radiotherapy novocain injection aspiration irrigation or puncture and of operative removal of the calcareous material are reported

Calcareous degeneration in the tendon cuff of the shoulder is a frequent and disabling lesion The accompanying subdeltoid bursitis is a secondary condition The symptoms and signs and the roentgenographic features of this lesion are characteristic The degeneration is probably due to attrition from the use of the arm at the side with repeated sudden jerky movements It may be prevented by avoiding such motions.

The calcareous material is suspended in liquid in the early acute cases and the roentgenographic shadow is cumulus cloudlike and

fairly homogeneous. The deposit is granular and infiltrating in the chronic cases and the shadow is fragmented and irregular in outline and density

Relief from pain and spasm and absorption of the suspended calcareous material may often be obtained in the early acute cases by rest heat, diathermy cold, ethyl chloride spray or radiotherapy The chronic cases usually are not helped

Massage stretching or manipulation are likely to increase the pain spasm and limitation and to damage the shoulder

Rupture of the calcareous deposit into the bursa spontaneously or with treatment will give immediate relief

Aspiration irrigation or puncture may relieve pain when thereby the material is drained and the tension reduced Novocain injection relieves pain only temporarily unless the cavity is drained at the same time

Operative removal of the calcareous deposit is the surest and quickest method of relief particularly in the chronic cases Complete removal of the deposit is desirable for best and permanent healing of the lesion

Special exercises should be used with any of the treatments for preservation and restoration of motion and strength in shoulder and arm

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THE FUNCTIONAL PATHOLOGY OF EXPERIMENTAL FROSTBITE AND THE PREVENTION OF SUBSEQUENT GANGRENE

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THE problem of tissue damage after exposure to severe cold is particularly timely since the number of cases of gangrene and death is increasing with the intensification of the war effort. Accordingly it seemed important to follow the effects of experimental and accidental exposure to low temperature by means of the fluorescein method which we reported some time ago (6, 7, 8).

The tissue changes occurring in frostbite have been carefully studied by German observers (4, 11) by Lewis and by Greene. These investigations have been summarized excellently by Bigelow in a recent survey so that a detailed review is unnecessary. However a brief summary of the available facts seems warranted.

Exposure to severe cold in the absence of marked dampness causes an immediate slowing of the blood stream owing to strong arteriolar constriction. Oxygen exchange ceases since the dissociation of oxyhemoglobin at low temperatures is negligible. If the cold is sufficiently intense the frozen limb solidifies completely. This happens at a temperature lower than anticipated due to the effect of supercooling. In man as well as in experimental animals, the skin becomes very white, a state which persists until thawing starts. A biopsy during this stage fails to reveal any essential change in the tissue save for the extreme contraction of the arterioles; this may be greater *in vivo* than in biopsies. Immediately after thawing the skin may remain pale. This may be explained by persistent arteriolar spasm since biopsies obtained at this time fail to re-

veal any structural reason for the lack of circulation. A fluorescein test performed at this time shows an arrest of circulation with absence of fluorescence in the area previously cooled. In $\frac{1}{2}$ hour after exposure the skin becomes bright pink. Apparently some substance forms during the exposure and causes maximal capillary dilatation. Subsequently swelling of the exposed area produces a considerable increase of size. After an indefinite time the swelling subsides and complete healing occurs or gangrene begins, initially as blue brown areas of discoloration and subsequently in all the exposed areas.

During this phase our own biopsies and those of many other observers (1, 3) show the following characteristics. After 24 hours the endothelium of the arterioles is swollen and spongy. The lumen of many vessels contains clumps of red blood cells with no tendency for them to adhere to the wall or to organize. The structure of the erythrocytes is intact. Much later, 72 hours or more, real thrombosis develops; this may be due to massive infection which occurs almost always in severe frostbite unless great care is taken to prevent the invasion of bacteria. At this time the tissue cells stain poorly and cell membranes undergo dissolution. Later all differential staining qualities are lost and many vessels are filled with clumps of red blood cells or thrombi. The photographs of Greene show this in a superlative manner. It is undecided whether the clumping called stasis (10) or *sitting* (3) results from loss of plasma into the tissues and stranding of the red blood cells or from colloidal chemical changes. The problem was not deemed essential in the present studies since fluorescein affords a clear insight into the physiology of these vessels.

Mild cold. Six normal individuals were chilled mildly by immersing the arm up to the

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Aided by grant from the John and Mary R. Markle Foundation and the Council on Pharmacy and Therapeutics of the American Medical Association.

elbow for 8 minutes to produce a skin temperature of 10 degrees C. At this time 10 cubic centimeters of a solution containing 5 per cent fluorescein and 5 per cent sodium bicarbonate were injected intravenously and the lights of an otherwise dark room were extinguished. The cooled area bright pink in daylight is exposed to the special ultraviolet light which causes fluorescein to emit its specific golden-green fluorescence. The cooled area shows a marked diminution of fluorescence in comparison to normal skin as long as the temperature of the exposed area is reduced. The examination of capillary blood removed from an area of diminished staining shows that it contains as much fluorescein as blood in other parts of the body. This fact suggests that the dye cannot diffuse from the cooled capillaries into the interstitial spaces in the same way as in unaffected areas of the skin. This may be due to decreased capillary permeability or markedly decreased filtration pressure. In respect to filtration pressure it should be noted that neither local anesthesia nor sympathetic block changes the picture. A patient with a complete transverse lesion of the spinal cord (6th dorsal) showed an identical reaction when his feet were exposed to cold. If arteriolar contraction were induced by an axon reflex and would thus decrease filtration pressure and thereby diminish tissue staining it is difficult to understand why large doses of nitroglycerin or amyl nitrite sufficient to cause a marked fall of blood pressure do not change the picture. Even a decided increase of intra-capillary pressure by the application of a blood pressure cuff with a pressure of 70 millimeters of mercury proximal to the cooled area and the augmented venous pressure induced fails to alter the picture. Therefore one is forced to assume that the first reaction to cold is a decrease in capillary permeability with parallel arteriolar contraction to decrease filtration pressure. This might be interpreted as a defense mechanism which prevents water from entering tissue spaces and averts tissue bursting at freezing temperatures. The same results were obtained in 11 rabbits when mild cooling was induced in previously depilated areas. A detailed report of these observations was published elsewhere (5).

Freezing In 6 rabbits severe cooling was produced by applying beakers 3.7 centimeters in diameter and filled with dry ice to the depilated skin of the abdomen for periods ranging from 5 minutes to 90 minutes. Ordinarily 5 beakers were applied in an experiment and the intervals were so arranged that the end of the cooling period was simultaneous for all. This permitted simultaneous observation of the vascular effects after varying degrees of damage.

Seventy-five one-hundredths of a cubic centimeter of the aforementioned fluorescein solution were injected intravenously immediately after a cooling period. At this time all exposed areas were frozen stiff. The entire abdomen becomes intensely fluorescent under long wave ultraviolet light save in the areas exposed to cold. The latter remain deep purple indicating their complete exclusion from the circulation. At intervals varying from 7 to 58 minutes and depending upon the duration of exposure as shown in Table I all areas become fluorescent. This event occurs a *considerable time* after the tissue has thawed. Fluorescence in the cooled areas slowly becomes more intense than in the surrounding areas and finally they are decidedly hyperfluorescent in comparison to the normal tissue. The picture closely resembles that of an inflammatory area. The marked staining is the result of increased capillary permeability subsequent to the anoxic phase of freezing. *Complete fluorescence was always temporarily restored in an exposed area* despite extreme exposure to cold. Then previously frozen areas begin to swell and they present a bright pink color in daylight.

Since fluorescein is excreted rather rapidly the test can be repeated after 12 hours. At this time the picture has usually undergone a complete change. Areas frozen for short periods show a fluorescence like that of the other skin. If the area has been exposed for a long period patches of nonfluorescent skin are seen and indicate a pregangrenous state. These patches may not be detected in ordinary daylight.

After 72 hours the part exposed to freezing temperature for long periods again shows complete nonfluorescence just as it did immediately after freezing. This fact indicates vascular occlusion which will result in gangrene.

Biopsies from such nonfluorescent areas show arteriolar stasis with packed red blood cells and loss of differentiation of the cell elements as prominent features.

Since most severe exposure with solidification of tissue is always followed by a period of complete restoration of circulation for a period of 6 hours or more it seemed promising to attempt to prevent the formation of clots by heparinization subsequent to exposure. This was done in 5 rabbits of corresponding weight and for the most part from the same litter as the controls. They were chilled with dry ice in the manner described earlier. Five other rabbits served as controls. The treated rabbits obtained 3 cubic centimeters of heparin (10 milligrams per cubic centimeter) intravenously every 12 hours beginning $\frac{1}{2}$ to 3 hours after freezing ended. These injections were continued for at least 5 days.

Superficial gangrene involving the entire thickness of the skin but not the underlying fascia was obtained regularly in all exposed areas of untreated controls when the exposure to dry ice lasted more than 15 minutes. Some developed partial or extensive gangrene with shorter exposures.

In the group which received heparin clotting time was determined by the Lee White method; it never went below 22 minutes in any animal. The swelling of the previously exposed areas was constantly greater in this group than in the untreated animals. The exposed areas remained fluorescent and gangrene did not occur. Two animals did show small superficial areas of necrosis within the exposed area after exposures of 45 and 60 minutes respectively.

Nevertheless all animals showed a marked susceptibility to infection of the previously frozen area, especially when gangrene did not develop. Tightly applied sterile dressings from the outset and reapplication under absolutely sterile conditions as employed successfully in the treatment of burns solved this problem. In subsequent experiments the exposed area was painted with an aqueous solution of merthiolate and the sterile dressings were coated with 5 per cent sulfathiazole ointment in order to prevent infection of the oozing tissue from occurring.

TABLE I.—DEPILATED SKIN OF RABBIT ABDOMEN EXPOSED TO FREEZING BY CONTACT COOLING WITH BEAKERS FILLED WITH DRY ICE

Time of exposure to beakers filled with dry ice Mins	Time of aortic vascular occlusion after exposure Mins	Time of complete restoration of circulation and onset of vascular occlusion Hours	End result
5	1	N occlusion	Healing
15		1	Small areas of gangrene
30	30		Gangrene of exposed skin
60	90	7	Gangrene of exposed skin

Encouraged by these apparently good results we exposed the depilated hind leg of 22 rabbits to severe cold while the animal was under nembutal anesthesia. The hind legs of the animals were covered to the knee by a boot of condom rubber and great care was taken to avoid any constriction. The prepared legs of 2 animals were then dipped simultaneously into an alcohol bath of -12 degrees to -20 degrees C for a period of 45 to 90 minutes. This cooling period corresponds to a much longer one in cold air for the convection of heat by alcohol is many times that of air. The thin layer of rubber made it for practical purposes a contact cooling. In 5 to 8 minutes the submerged portions of the legs were frozen stiff. One animal of each pair was untreated while the other was heparinized. Among 11 heparinized animals, 9 recovered completely in so far as tissue loss was concerned; two developed a superficial necrosis of considerable extent 3 days after exposure but they did not lose the leg. Two animals died from severe internal hemorrhage on the 4th and 5th day respectively after exposure. Their clotting times had gone to 16 and 18 hours.

All animals of the untreated group developed complete gangrene of the exposed leg with spontaneous amputation which included the bone.

All animals of both groups had an initial motor and a sensory paralysis of the exposed area except one of the heparinized group. Three of the heparinized frostbitten animals recovered motor and sensory function in about

2 weeks while another had complete loss of sensation as tested by pinprick for a period of nearly 4 weeks

In 2 of the heparinized group in which superficial gangrene occurred the moderate pressure from adhesive applied to one area might have been responsible. All animals of the heparinized group displayed full fluorescence of the damaged leg in each test throughout the period of observation

Accordingly complete gangrene of the tissue following severe experimental frostbite in rabbits can be prevented by heparin. The great danger associated with this treatment seems to be the marked susceptibility of damaged but surviving tissue to infection. Nerve tissue seems rather sensitive to cold and is less liable to survive without injury severe exposures. This may explain the persistent paresthesias and hyperesthesias after frostbite not attended by loss of tissue

In 4 animals a pressure bandage was applied after exposure to cold. Two of them received heparin as well while the remaining 2 were treated only by a pressure bandage. The result in the heparinized animals was the same as without pressure bandage whereas the animals treated by pressure bandages alone developed a rapidly spreading extensive gangrene like that seen in animals with ordinary dressings

Clinical evidence The value of the fluorescein test in estimating the extent of damage in patients with recent exposure to low temperatures was demonstrated in 14 cases of frostbite. Thanks to the collaboration of Dr Edward Bernecker, commissioner of hospitals of the City of New York, we succeeded in obtaining these patients from various New York hospitals immediately after they sought aid. The earliest was under treatment 7 hours after exposure and the latest was 48 hours. All cases occurred in February 1943 during one night when the weather suddenly turned very cold and a strong dry wind was blowing. There were 13 males and 1 female. The men were frostbitten while working on the docks; the woman was exposed while waiting for a bus. Five men had lesions of the hands as well as feet and 3 also had frostbitten ears. The woman had her most severe injury in the feet

All patients were subjected to a fluorescein test immediately after admission. The results of these tests were carefully recorded and compared with the final tissue damage noted after an interval of several days. Since the studies with heparin had not advanced sufficiently at that time no patients were treated with it. If the fluorescein test is done within the first 12 hours it does not perfectly reflect the tissue damage which may be anticipated. In 4 patients practically all the exposed tissue fluoresced fairly well indicating that the vessels were open at this time. Twenty-four hours later these patients showed large areas of nonfluorescence after the intravenous injection of fluorescein and these areas corresponded exactly with the loss of superficial tissue which occurred during the subsequent period of observation. If patients are seen 14 or more hours after exposure the fluorescein test reveals exactly the amount of superficial tissue damage to be expected. In 2 patients seen 14 and 16 hours after exposure a novocain block of the lumbar sympathetic ganglia was performed without any change in the fluorescein pattern indicating that no essential part of the circulation was blocked by spasm. One observation seems important. The fluorescein test indicates the tissue damage expected in the superficial layers. While this is a fairly good indicator of the vascular status of the deeper vessels in occlusive vascular diseases this does not hold for frostbite. In frostbite there may be extensive loss of surface structures despite little or no damage to deeper structures. Among the 14 cases only 1 required débridement of 2 toes while others had complete tissue restoration. It can scarcely be overemphasized that greatest conservatism is in order in respect to surgical intervention after frostbite. The ability of deeper tissues to regenerate is excellent after frostbite and the surgical principles employed in occlusive vascular disease are not applicable to cases of frostbite.

Like Davis and his collaborators we were unable to predict which cases would develop blisters and which would remain dry. Of the 14 cases 11 developed large vesicles. The content of these blisters after the fluorescein test seems to provide a good indication of the

status of the deeper tissues. Fifteen minutes after the injection of fluorescein, the amount of dye present in the blisters was large in all cases although the surrounding skin did not fluoresce. In 1 case the content of the blisters was free of fluorescein and this patient lost both toes on which the nonfluorescent blisters were located.

The functional pathology of animals exposed to severe cold and of patients suffering from frostbite seems to be the same. Since tissue loss can be averted in experimental animals by the use of heparin early after the exposure, this method holds promise in cases of frostbite.

SUMMARY

1. The tissue alterations after exposure to severe cold are described and the sequence of events as well as the vascular occlusion due to stasis is discussed.

2. The sequence of functional changes after exposure to mild cold as elicited by the fluorescein test, is described and emphasis placed upon the arteriolar spasm and decreased capillary permeability.

3. These vascular changes are independent of central nervous system influences and seem to occur by axon reflexes.

4. Cold sufficient to solidify the exposed tissues causes a complete interruption of circulation during the exposure. This is always followed by a period of complete restoration of circulation and increased capillary permeability as evidenced by the fluorescein test. This period lasts for 6 to 16 hours after exposure. This is the most promising period for therapeutic endeavors.

5. The period of circulatory restoration is followed by one with arteriolar and capillary

occlusion resulting from the formation of red blood cell clots. Gangrene of the associated area is the consequence.

6. Heparin administered during the period of circulatory restoration prevented gangrene in 16 rabbits whereas all controls had complete gangrene of the part. Five animals were exposed by freezing small areas in the remaining animals the entire hind leg was frozen.

7. Although tissue loss was averted by the early use of heparin sensory and motor nerve paralysis was often not prevented.

8. Fourteen cases of human frostbite show that the fluorescein test permits the exact prediction of subsequent superficial tissue loss provided certain precautions are taken.

9. Great surgical conservatism is in order in frostbite since these lesions show a marked tendency to heal. Moreover the rules for amputation in occlusive vascular disease are not applicable in frostbite.

10. After an injection of fluorescein the dye content of the blisters seems to afford a good insight into the vascular damage in the deeper structures.

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ACUTE PUTRID ABSCESS OF THE LUNG

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THIS paper is based on the 172 cases of acute putrid abscess of the lung which have been subjected to operation in the past 16 years at the Mount Sinai Hospital. Since there have been but 4 deaths in this series of cases operated upon in accordance with a definite plan, the operative procedures which have been advocated and employed can be regarded as well established and safe. In view of the fact that usually these cases are seen only in the preoperative and early postoperative phases, one of the two purposes of this presentation is to report on the late anatomic and functional results of operation. The other is to survey the essential features of the disease on which the one stage operation has been based.

The concept of acute putrid abscess of the lung as a surgical disease and the related evolution of surgical treatment are based on (1) an understanding of the pathology of acute pulmonary abscess with special reference to surgical features, (2) the application of roentgenography to the diagnosis and more particularly to the exact localization of pulmonary abscesses, (3) the development of a one stage operative procedure, (4) the evidence that consistently good and lasting results are obtainable by such an operation.

Occasional references in the literature indicate that there has been some general acquaintance with the pathology of putrid pulmonary abscess but it remained for the thoracic group of our hospital to present a clear picture of the pathology with special reference to surgical features. Since 1932 the pathology of acute putrid pulmonary abscess has been set forth by members of the group because it gradually became evident that treatment particularly surgical treatment had to be related directly to the pathology of the disease. Although all the features have not as yet been generally conceded to exist, I believe that the following essential ones now are rather widely

accepted. Omitting the rare metastatic form (which has its own distinctive features) all putrid pulmonary abscesses can be assumed to be due to aspiration of infective material. There is set up a gangrenous bronchopneumonia in the involved bronchopulmonary segment. Liquefaction occurs in a few days and an abscess is formed within a week or 10 days of the onset of the pulmonary infection. The brief period of evolution should be stressed in order to dissipate a belief which still prevails that the gangrenous pneumonic lesion is diffuse and often is only partially liquefied for a period of several weeks or longer. The abscess usually is fully developed within 2 weeks. In most cases an acute abscess is of substantial proportions and thus accounts for the common initial expectoration of a considerable quantity of foul pus. The abscess is single and spherical, is always situated superficially within the pulmonary lobe and abuts on the thoracic parietes. The shell of lung between the abscess and the pleural surface usually is thin, compressed and avascular. The abscess cavity is well demarcated from the beginning. Its contents are foul air, pus and debris and in the early stages fragments of gangrenous lung. The interior of the cavity is smooth at a surprisingly early stage. There are present invariably the orifices of one or more bronchi. The feature of perhaps greatest surgical moment is the constant occurrence of well defined pleural adhesions over the abscess which usually seal off effectively the free pleural space. These adhesions are visceroparietal in the great majority of cases, bind the abscess to the thoracic parietes, and render it readily accessible for safe surgical entry. In a small proportion of cases the abscess faces a fissure, the diaphragm, the mediastinum or the pericardium. Under these circumstances there are also overlying adhesions which however are local and may not extend to the parietal pleura. It is probably this variety of abscess which has led to the erroneous concept of central abscess of the lung.

Address delivered to the House Staff of the Mount Sinai Hospital, July 6, 1944.

Early in our studies it became evident that a differentiation between acute and chronic abscess was necessary. It was noted repeatedly that the abscess usually retained for a period of several weeks the characteristics I have outlined. Towards the end of or after 6 weeks, additional lesions usually appear multilocularly spread of infection by spill over interstitial pneumonitis fibrosis, bronchiectasis. These are the features which often render the results of surgery less satisfactory in respect to mortality, morbidity and cure. Accordingly we decided to term all abscesses acute if of less than 6 weeks duration with the idea of solving the problem of putrid pulmonary abscess within that period. Obviously this is a rather arbitrary classification and we like others have noted that occasionally abscesses remained simple after 6 weeks or on the other hand became complicated in a few weeks. Nevertheless it appears to be the best classification at least from the viewpoint of therapy for our results have been decidedly less satisfactory in the second 6 weeks period (that of subacute or subchronic pulmonary abscess). Other classifications have been proposed of which the most popular appears to be the division into simple and complicated abscess based on pathology. It is difficult to determine where the line should be drawn in such a classification. Furthermore emphasis is omitted on the aspect of therapy in the acute stage and no advantage is offered other than a statistical explanation of good versus poor surgical results.

Related to the question of classification is that of the indication for operation for acute abscess of the lung. Not all patients with acute putrid abscesses who enter this hospital are operated upon but it can be said that operations have been more often performed in recent years because consistently good results were observed. The indications for operation for acute abscess may be imperative or elective. Among the former are patients with hyperacute manifestations (severe toxicity) unusually large abscesses and abscesses which appear to be on the verge of invading or have already invaded the pleura. In a substantial proportion of cases the indications are elective. These are cases of small abscesses which remain station-

ary or increase in size after a period of observation abscesses in which cavities drain poorly (roentgen evidence) patients with sustained fever or intensely fetid sputum cases in which there is diabetes. Not all elective indications need be enumerated and it can be stated that spontaneous subsidence might have (would have?) occurred in some of the patients who have been subjected to operation.

The application of roentgenology to the diagnosis and especially to the exact localization of an acute abscess represents the essential basis for correct surgical management. After it was learned that films revealed the characteristic feature of pulmonary abscess (cavity with a fluid level) in no more than half the cases that only a circumscribed area of dense pneumonic infiltration existed in some cases and that areas of rarefaction might or might not appear in the midst of such infiltration during observation. It became evident that the diagnosis of pulmonary abscess often could not be made on films alone. On the other hand studies of films always made possible a precise localization of the abscess. Hence every effort was bent in the latter direction in order to determine in any given case the site at which the abscess abutted on the thoracic parietes and thus the site at which the abscess could be entered safely through adhesions. Theoretically a study of films taken in various positions including the oblique should provide the required information. Actually there are not infrequently errors in interpretation particularly when abscesses are situated laterally on the bend of the thoracic cage. Adding to the foregoing the difficulty in counting ribs accurately it became apparent that a marker for precise localization was required. This was provided by the spot method introduced by Rabin which is employed immediately before operation. A mixture of methylene blue and iodized oil is injected into the intercostal musculature at the assumed place (often determined fluoroscopically) of contact between the abscess and the thoracic wall. Films in appropriate positions are taken and the relationship of the iodized oil to the abscess is seen. The methylene blue in the musculature is exposed at operation in order to locate the situation of the

radiopaque oil which was injected. The relationship of the oil to the abscess being known the operative exposure of the abscess is performed in accordance with the relationship of the 'spot' to the roentgen shadow of the abscess. Thus the spot may be immediately over the abscess or as much as an inch from the site of contact between abscess and parietes. In the rare instances in which the method has failed the reason was to be found in an error in technique (failure to inject the intercostal musculature). The Rabin spot method can be employed with advantage in all cases but in any event should be used when ever the exact place of contact of the abscess with the thoracic parietes is in doubt. Emphasis should be placed on its use in seriously ill patients because the abscess should be entered with minimal dissection in such cases.

The development of the one stage operative procedure was based on the realization that a pulmonary abscess is characterized by a superficial position with overlying adhesions and that the essential pathology is constant. Many operations performed in our clinic have established the correctness of both points. They have also disclosed errors which required correction. Thus when adhesions are not encountered one can be quite sure that the site of surgical approach is not correct. Again if the abscess is not found by exploratory aspiration superficially in the lung the needle has been introduced at an incorrect point. With the full knowledge of the pathology and with lessons gleaned from errors like the foregoing the logic and desirability of the one stage operation became more and more apparent. We proceeded in a direction diametrically opposed to the two stage operation which was and still appears to be rather generally practiced. The two stage operation is based on the assumption that liberal exposure of the abscess is required and that adhesions if present are not apt to be sufficient to prevent contamination of the free pleural space when the abscess is drained. The so called central abscess also figures in the two stage operation. The disadvantages inherent in the two stage operation need not be set forth. It is not amiss to state however that a two stage operation is preferable to a one stage

procedure which is not based on precise roentgen localization of the abscess. There has been no change in the principles of the one stage operation which we have been performing for 16 years or longer. In brief they consist of the exposure of pleural adhesions by a limited excision of a segment of one rib (in most cases) incision through adhesions at their densest portion (at which place the bulge of the abscess will often be noted) dis closure of the abscess by aspiration its unroofing by excision of the thin compressed shell of overlying lung and the visualization and gauze tamponade of the abscess cavity and all its recesses. In a small proportion of cases parietal adhesions will be scanty or absent (interlobar abscess etc.). Under these circumstances the one stage operation is carried out by suturing normal lung around the abscess to the thoracic parietes and after the free pleural space is securely shut off by entering and unroofing the abscess. The principles of operation remain the same whether an abscess is either single or multilocular and whether the patient is either seriously or mildly ill.

There is scarcely any surgical experience which compares with the dramatic result which is seen in virtually all cases following the one stage operation. In a patient who often is toxic or septic and expectorating fetid pus cough and expectoration cease promptly fever subsides and the general appearance is one of great improvement. Indeed the continuation of symptoms of pulmonary abscess such as the expectoration of foul sputum is evidence that the pulmonary abscess has not been adequately cared for at operation. The immediate results of operation thus are excellent. Concerning the 4 deaths in 172 operative cases at least 2 are ascribable to errors in technique and probably were avoidable. Hence the mortality of operation for acute putrid pulmonary abscess should be ascribable to the operation and only rarely to the disease. Few secondary operations for drainage of adjacent areas of pulmonary suppuration or for empyema have been required in recent years due to improvement in methods of localization of the abscess as well as in the technique of operation. The

rapid recession of clinical manifestations usually is attended by roentgen evidence of subsidence of the inflammatory reaction around the abscess cavity. The latter soon becomes clean and presents on its floor the orifices of one or more bronchi. The chief problem after operation has been the maintenance of the pulmonary cavity and more particularly of the bronchial fistula. The tendency is to permit the fistula and the wound to close too soon. Experience has shown that the bronchial fistula should be maintained until the patient is entirely symptom free and pulmonary infiltration (x ray evidence) has virtually disappeared. In this postoperative period usually of 4 to 8 weeks' duration the wound requires meticulous attention to detail.

The follow up which now extends over a period of 16 years reveals that recurrence of pulmonary abscess rarely if ever takes place. The few instances in our series of so called recurrence of putrid pulmonary abscess probably represent persistence of the infection and can be ascribed either to inadequate unroofing at the time of operation or to premature closure of the wound. Most pulmonary cavities heal even when large but there arises occasionally the problem of an unusually large cavity which remains after the unroofing of an

abscess. Some of these large cavities heal in time. Others require some type of plastic procedure for their closure. Various methods have been advocated. I have devised a simple procedure that of free fat transplantation for the purpose. The results usually are satisfactory but occasionally the graft is extruded or there remains a closed dead space following absorption of the graft.

In any follow up continued over a period of many years patients may be well of their disease but die from other causes. Not all the patients who were cured of their abscess are alive today. There have been deaths from a number of unrelated causes (cancer of the stomach, suicide, etc.) There were also 2 deaths following operations for the drainage or closure of ancient cavities left after the primary operation. The follow up which includes all the operative cases has revealed that the great preponderance of patients not only have healed wounds and show complete healing of the abscess, but also remain symptom free permanently. Thus the one stage operation can be regarded as entirely satisfactory for acute pulmonary abscess providing not only a very low operative mortality and good immediate results but also a high incidence of permanent cure.

GASTRIC RESECTION FOR DUODENAL ULCER

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TWENTY TWO years ago the Mount Sinai Hospital group for gastroenterological surgery began to discard gastroenterostomy in favor of partial gastrectomy in the surgical treatment of duodenal ulcer. We had been impressed by Haberer's publication which had shown that gastric resection for duodenal ulcer could be performed with a reasonably low mortality. Furthermore the frequency of gastrojejunal ulcers after gastroenterostomy (in our material 34 per cent among these 18 per cent proved by reoperation) had convinced us that gastroenterostomy was an illogical operative procedure. It is a generally accepted fact that gastroenterostomy does not reduce hyperacidity to any marked degree in the vast majority of patients. In addition each patient has before him the possibility of the development of a gastrojejunal ulcer. Furthermore it is important to remember that many patients after a gastroenterostomy continue to complain of gastric distress although they are not suffering from a gastrojejunal ulcer. I feel certain that not more than about 20 per cent of the patients suffering from a non-obstructive duodenal ulcer are permanently free of symptoms following gastroenterostomy. 80 per cent of failures should condemn any operation.

A number of years before Haberer's publication the well known British surgeon Bland Sutton in a Hunterian lecture pointed out that in the presence of an open pylorus, gastroenterostomy would not cure a duodenal ulcer. "With an unobstructed pylorus gastroenterostomy cannot be relied upon to cure a chronic duodenal ulcer and as it exposes the patients to the discomforts and risks of regurgitant vomiting of jejunal ulcer I have gradually abandoned it as a routine method and prefer to excise the pylorus and the segments of the duodenum containing the ulcer."

In other words Bland Sutton suggested pylorectomy combined with removal of the ulcer bearing area of the duodenum rather than

gastroenterostomy in the treatment of an obstructed duodenal ulcer. However Haberer went a step further. He showed that in order to attain permanent relief of symptoms removal of at least half the stomach rather than pylorectomy was advisable. This more radical operative procedure was supported by the work of Lorenz and Schur who had shown that extensive resections of the stomach were necessary in order to effect a marked reduction of the preoperative hyperacidity.

Hyperacidity and duodenal ulcer are closely interwoven. If we had some drug at our disposal which would make a hyperacid stomach anacid without destroying the gastric mucosa we would have a simple nonoperative solution for the cure of nonobstructing duodenal ulcer.

It must be admitted that gastric resection while far superior to gastroenterostomy does not cure every patient suffering from duodenal ulcer. A small percentage seems resistant to any form of surgical therapy. Their number is not large however and should not reach above 5 to 10 per cent following a properly executed gastric resection. However because of this small group of failures in contemplating the overall picture of partial gastrectomy for duodenal ulcer it would be most unreasonable to consider discarding the operation.

The extent of the gastric resection has been gradually increased because there seems to be a close relationship between the amount of stomach removed and the postoperative results. Originally surgeons who encountered a duodenal ulcer in a very movable duodenum would remove the pylorus and the first part of the duodenum (v. Rydygier, Bland Sutton). In other words they performed a pylorectomy. It was soon found however that neither pylorectomy nor antrumectomy (the next step) produced any marked reduction in the gastric acidity. For this reason the gastric resection was extended beyond the reentrant angle (partial gastrectomy) or even to

a level close to the cardia (subtotal gastrectomy)

I am amazed at the frequent abuse of the term 'subtotal gastrectomy' for duodenal ulcer. The classification 'subtotal gastrectomy' implies that the upper line of resection is located near the cardia and that the lower line reaches below the duodenal ulcer. Practically no gastric resection for duodenal ulcer reaches as far as the cardia. The line of transection during gastric resection for duodenal ulcer is situated slightly above the re-entrant angle. It seems that the correct term should be partial gastrectomy. On the other hand gastric resections for gastric ulcer are usually subtotal gastrectomies.

I would like to make this point very clear as it is of greatest importance in the statistical evaluation of late results. It has become the custom for some surgeons in recent years whenever the ulcer infiltrates the pancreas or is imbedded in extensive adhesions, i.e. when ever the removal of the ulcer bearing part of the duodenum presents any technical difficulties to leave the ulcer *in situ* and carry the transection just above not below the ulcer. Anybody who has operated upon many patients having these complicated conditions knows that in order to insure a safe closure of the duodenum the surgeon in attempting to leave the ulcer *in situ* is often forced to leave part of the pylorus on the posterior wall even if he does not perform a typical prepyloric Finsterer operation (*Resektion sur Ausschaltung*). Yet these incomplete operations are erroneously called subtotal gastrectomies. Everybody familiar with the literature realizes the importance of the pylorus in the question of recurrent duodenal or gastrojejunal ulcer. It is obvious that if these incomplete operations are labelled subtotal gastrectomies, the follow up results will be clouded. The operation is accused whereas the technique is actually at fault. In a typical gastric resection the specimen must show a complete ring of duodenum.

The complete removal of the pylorus in gastric resections is of the greatest importance in obtaining a satisfactory postoperative result. Seventeen years ago Haberer published a case in which the pylorus had been left *in situ*

(Finsterer operation). Subsequently a number of secondary gastric resections for gastrojejunal ulcers were performed. Finally the patient was cured when the pylorus was removed. Similar recurrences may be observed even if only part of the pylorus is removed at the time of operation.

Resection of the duodenum above the lesion with complete removal of the pylorus is usually feasible in those cases only in which the ulcer is located beyond the first portion of the duodenum and in which it encroaches upon the common duct. In these cases removal of the ulcer would present too many serious technical difficulties to warrant increasing the risk. However ulcers in this location are fortunately rare. Most duodenal ulcers are resectable when the proper technique of freeing of the duodenum is employed. The recent trend in some hospitals of leaving the ulcers in place should not be encouraged. It represents a make shift procedure rather than a method of choice.

If the line of dissection in the duodenum is carried above the ulcer and not below the ulcer the operative procedure should be classified as 'palliative resection of the stomach'.

Adoption of the operation of partial gastrectomy for duodenal ulcer came about very gradually. Strong opposition was encountered not only from those surgeons who preferred gastroenterostomy because they were unable to perform gastric resections but also from leaders in the profession. It seemed to me that when we first tried to introduce this method in this country we not only found practically no support but we had to apologize for introducing so radical a procedure. Since then the picture has changed completely and now gastric resection is considered by most surgeons as the method of choice in the treatment of duodenal ulcer.

Here and there we still find small groups who continue to offer resistance. In 1936 Trimble and Reeves stated "No extravagant claims are advanced for gastroenterostomy. It is not a panacea for all gastric and duodenal ulcers. Nevertheless, it is felt that this operation should be applied in the majority of these lesions occurring as they do in the pyloric portion of the stomach and the first

portion of the duodenum and that it is one of the most satisfactory operations in the armamentarium of the surgeon

Recently Heuer published a careful statistical review based on a study of the gastric and duodenal ulcers at the New York Hospital. He comes to the amazing conclusion that gastroenterostomy is a satisfactory operation not only for duodenal but also for gastric ulcers. He recommends this method to his students. As his service represents one of the important surgical teaching units in this country, his conclusions should not go unchallenged.

Heuer bases his opinion as to the limited value of gastric resection in the surgical treatment of gastric and duodenal ulcers when compared with results following gastroenterostomy on the very small number of 83 resections for duodenal ulcers and 59 resections for gastric ulcers. In view of the fact that the present popularity of gastric resection for gastroduodenal ulcers is based on the experience collected all over the world on hundreds of thousands of cases, these 142 cases seem particularly insignificant. If we want to revert to the antiquated operation method of gastroenterostomy, one's opinion should be supported by the analysis of a substantial number of patients and not by so small a group. Heuer mentions the small inherent operative mortality of gastroenterostomy and stated that 100 consecutive gastroenterostomies were performed on his service since 1939 without a death. But Duval and Wilson have reported 105 and 93 consecutive cases respectively of gastric resection for ulcer without a death. The average mortality of gastroenterostomy is about 2 per cent, just about the same as the mortality following gastric resection. Thus the argument that the mortality of gastric resection when performed by well trained surgeons is higher than that of gastroenterostomy is fallacious.

Heuer has collected a large number of undifferentiated ulcers, both gastric and duodenal ulcers (12,306 treated by gastric resection and 5,715 by gastroenterostomy) operated upon by different surgeons in different countries between 1935 and 1942 with a quotation of their mortality rates. No references are

given. It is quite evident that no conclusions of any value can be drawn from such a statistical study because operative technique changed materially during this period. The better preoperative preparation of the patient, the introduction of continuous spinal anesthesia, the use of the sulfa drugs and the recent popularity of blood transfusion fall into this period (1935-1942). They have reduced postoperative mortalities considerably. Thus it is unfair to compare operative results in 1935 with those in 1942.

Follow up results after gastric resection for gastric ulcer are excellent. Mage has reported among 98 cases of gastric resection for gastric ulcer performed at Mount Sinai Hospital, one instance of a gastrojejunal ulcer. The patient had repeated attacks of epigastric pain and vomiting. The x-ray examination showed a small irregular penetration suggesting a lesion in the postoperative stomach. The patient was not operated upon again and was lost from observation after 18 months. In view of the extreme rarity of a gastrojejunal ulcer following subtotal gastrectomy for gastric ulcer and in view of the lack of substantial evidence, this case should not be included in the group of recurrent ulcers. On the other hand, it is generally conceded that gastroenterostomy for gastric ulcer is an illogical operation and that the follow up results are most unsatisfactory. I have followed many cases of subtotal gastrectomy for gastric ulcers over a period of 30 years and I have never observed one instance of gastrojejunal ulcer. Gastroenterostomy for gastric ulcer was discontinued by most surgeons many years before gastric resection was introduced as the operation of choice for duodenal ulcer. No amount of argument, no amount of statistical evaluation will bring gastroenterostomy back in the surgical treatment of gastric ulcer.

It is well known that results following gastric resection for duodenal ulcer do not approach perfection. Yet the results are so far superior to those following gastroenterostomy that the latter operation has been generally abandoned in the resectable duodenal ulcer group. It will never be possible to define which ulcer is resectable and which is nonresectable. An ulcer which appears nonresect-

able to one surgeon might be removed successfully by another surgeon

It is very difficult to compare late results and evaluate different methods published by different clinics. If a service uses gastroenterostomy in many cases and reserves gastric resection for ulcers which are easily removable the mortality should be lower than if gastroenterostomy is the rare exception as an operative procedure. Furthermore methods of follow up vary considerably in different hospitals. For instance many clinics base their follow up results on letter writing a most unsatisfactory method.

When we reached the conclusion that gastroenterostomy which we had used for many years was an unsatisfactory method we decided that in order to obtain an actual appraisal of the situation we would insist on personal interviews with the patient, supported when ever indicated by x rays and gastric analysis. When I summarized the results (9) of our 5 to 10 years follow up I found that 34 per cent of the patients suffered from a gastrojejunal ulcer 18 per cent were definitely proved when the gastrojejunal ulcer was found at reoperation. The remaining 16 per cent were based on clinical symptoms and x ray findings.

In those days (about 20 years ago) few hospitals had effective follow up systems. In fact most surgeons relied on general impressions not on accurate data. Our figures were therefore subjected to sharp criticism. It was stated that we did not know how to perform a gastroenterostomy properly. The fact that the vast majority of our patients were Jewish was given as the reason for the high incidence of gastrojejunal ulcers. However during the succeeding 10 years when other clinics introduced careful follow up systems, the correctness of our figures was established. Some clinics showed an even higher incidence of gastrojejunal ulcer. The pendulum swung so strongly in favor of gastric resection for duodenal ulcer that gastroenterostomy is now an operation of expediency not one of choice.

After we had published our findings with respect to the incidence of gastrojejunal ulcer following gastroenterostomy we began to compare the postoperative gastric acidity following gastroenterostomy with that following

gastric resection. The findings were most impressive. Whereas among 62 cases of gastroenterostomy we (10) had an incidence of 3 per cent anacidity there was an incidence of 66 per cent anacidity among 49 gastric resections (11). These figures were obtained with the Ewald test meal before the more accurate Rehfluss test meal was introduced. However the marked difference between 3 per cent and 66 per cent is of definite significance. The great value of gastric resection in the reduction of hyperacidity was evident in 8 patients whose histories I published from Dr. A. A. Berg's service (10). These patients had free hydrochloric acid varying from 20 to 68 following gastroenterostomy. When later re-examined after a secondary gastric resection for gastrojejunal or persistent duodenal ulcer they all showed complete absence of free hydrochloric acid—truly an *experimentum in vivo*.

When we published our figures of 34 per cent of gastrojejunal ulcers following gastroenterostomy we were told that after sufficient time had elapsed we would undoubtedly observe the same percentage of gastrojejunal ulcers following gastric resection. If the same careful follow up methods were used. This question can now be answered definitely in the negative. Mage has reviewed the material of the gastroenterological surgical group at Mount Sinai Hospital between 1923 and 1940. He studied 502 cases of gastric resection for duodenal ulcer and reports 2.5 per cent of gastrojejunal ulcers found at reoperation and another 5.5 per cent based on clinical evidence only. Thus the figures of 18 per cent (found at operation) and 34 per cent (diagnosed either by operation or clinically) of gastrojejunal ulcer after gastroenterostomy can be compared with those of 2.5 per cent and 8 per cent, respectively following gastric resection. It seems that these comparative figures tell the whole story and indicate clearly the superior value of gastric resection.

Mage has included among the 40 gastrojejunal ulcers 7 which had severe painless gross hemorrhage with negative x ray findings. It is doubtful whether these cases should be included among the group of recurrent ulceration. I mention this group only in order to

show that Mage a figure of 8 per cent of gastrojejunul ulcers following gastric resection for duodenal ulcer including as it does some doubtful cases can be considered as definite and conclusive evidence of the marked reduction (34 per cent to 8 per cent) in the number of gastrojejunul ulcers as a sequela of gastric resection as compared with gastroenterostomy.

In a previous paragraph I discussed the abuse of the term 'subtotal gastrectomy'. I have pointed out how misleading the indiscriminate use of this classification is and how easily it leads to misinterpretation and misinformation. I would like to say here a few words about another abuse which has found its way in recent years into the description of operations namely the term 'healed ulcer'. Every surgeon even the most experienced knows the difficulties of exact palpatory findings. The surgeon may feel sure that he is dealing with a small duodenal ulcer whereas the specimen fails to show any sign of an ulcer. When these cases are described as 'healed ulcers' instead of as showing no sign of ulcer a proper statistical evaluation of the material becomes impossible. Healed ulcers never heal completely without leaving some sign of scar formation or remnants indicating the previous presence of an active ulcer which can be demonstrated by the pathologist either macroscopically or under the microscope. When the pathologist reports completely normal findings the surgeon has no right to speak of a 'healed ulcer'.

In recent years a number of authors seem to have rediscovered the antecolic method of connecting stomach and jejunum. This method represents the oldest form of gastroenterostomy. When Woelfler performed the first gastroenterostomy in 1881 he used the antecolic method without enteroanastomosis. Eleven years later Jaboulay combined antecolic gastroenterostomy with enteroanastomosis in order to establish a better drainage of gastric contents.

Comparison of statistical material from different clinics is very difficult because the basic facts vary so much. This holds true not only for follow up statistics, but also for mortality statistics. One clinic will make frequent use of gastroenterostomy and reserve

gastric resection for the easily resectable cases, whereas another clinic will use gastric resection in practically every instance. Frequent use of gastroenterostomy should not be encouraged as a high percentage of patients thus treated are apt to suffer within a few years from gastrojejunul ulcer. It is very easy to keep the mortality for gastric resection for duodenal ulcer at a low level by the frequent use of gastroenterostomy. I have recently seen reports from two hospitals one performing gastroenterostomies in 21 per cent of the cases and the other in even a higher percentage 41 per cent. Such extensive employment of gastroenterostomy is inadvisable because some patients will later succumb following a subtotal gastrectomy for gastrojejunul ulcer which operation has a higher inherent mortality than primary gastric resection for duodenal ulcer. The surgeons at the Lahey Clinic hardly ever use gastroenterostomy in the surgical treatment of duodenal ulcer. They have performed 235 consecutive gastric resections for gastric duodenal or gastrojejunul ulcers with a mortality of 2.7 per cent. In this series 152 resections for duodenal ulcers were followed by 5 deaths 3 per cent.

Wilson has reported 250 gastric resections for peptic ulcers (gastric duodenal gastrojejunul and those complicated with gross and massive hemorrhage) with a mortality of 2.8 per cent. In 7 additional cases palliative procedures were carried out. Drainage was used in very few exceptional cases.

One of the best statistics has been published by Koennecke who performed between 1904 and 1931 468 gastric resections for ulcer with a mortality of 1.5 per cent.

It is very evident that the mortality has decreased materially within the past 5 to 10 years. While formerly a mortality of 5 per cent seemed reasonable evidently a mortality of 2 to 3 per cent is at present within reach of any surgical group trained for this special work. We should stop talking about the inherent high mortality of gastric resection for ulcer. The mortality of gastric resection should not be higher than that of gastroenterostomy if the operation is done by experts if it is higher we should blame the surgical technique and not the method.

Another fallacious argument is the assumption that ulcers vary in different countries. When we tried to introduce gastric resection in this country we were told that this major operation might be good for European ulcers but that gastroenterostomy was an excellent operation for the much milder ulcers in this country. Time has proved the fallacy of this argument. In the same way I believe that the operative material in our large cities throughout the country does not vary and offers the same operative risks.

SUMMARY

Gastric resection is at present the most popular method in the surgical treatment of duodenal ulcer. However occasional attempts are made to put the clock back and to reintroduce gastroenterostomy. The term partial gastrectomy should be applied to the operation performed for duodenal ulcer. The difficulty of comparing statistics from different hospitals is discussed. We cannot classify a case as a healed ulcer unless the specimen

shows evidence of a previous ulceration. The mortality following gastric resection for duodenal ulcer has been reduced in recent years. It is now as low as that of gastroenterostomy.

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ACTIVE MOTION BY MEANS OF OCCUPATIONAL THERAPY IN THE TREATMENT OF FRACTURES

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IF the standard textbooks dealing with the treatment of fractures are consulted there is usually an accurate description of the various methods used by the author for the treatment of a particular fracture and at the end of the description in rather a slurring or brief paragraph the author discusses the most important part of the treatment with such description as active motion is started in the fourth week or physiotherapy is started at once. These terms do not convey much to the student or the practitioner as they have become meaningless without some description of the *modus operandi* of these procedures. The same reaction is true in reading or listening to papers on the subject of the treatment of fractures. Most of us will concede that the early return to function is at least as important as an accurate anatomical alignment. Boehler has certainly stressed early return to function by the use of the walking cast but in reading his text it becomes obvious that he never forgets the principle of complete immobilization until firm union occurs. This principle must be closely adhered to under any and all circumstances otherwise failure is sure to occur. The time element must not be dogmatically stated because all of us have seen fractures which in an average individual will unite firmly in perhaps 8 weeks yet in some patients will take 12 weeks. Union must be actually determined by both clinical and roentgenological evidence and when there is a doubt immobilization should be maintained until that doubt is gone.

What has happened to the advocates of passive motion? In the not so distant past, the so called after treatment consisted of active and passive motion baling and massage. In a short time passive motion was abandoned because the careful observer often saw actual damage and retardation of the sought for result. Passive motion actually did more damage to the joint and muscles than was pro-

duced by trauma at the time of the original injury. Now it can safely be said that at no time should passive motion be used in the treatment of fractures. The subject of baling and massage is very elaborate and there are still many clinics which use this form of physiotherapy exclusively for restoration of function. On careful questioning and observation I find that most men today believe that baling and massage are of practically no value as far as functional return is concerned and certainly that vigorous massage can produce deleterious results which definitely retard an early good end result. The newer fads of course are diathermy and short wave therapy applied to the injured part. Again on the basis of my observations these modalities do not assist the patient to get function. At best they may cause the subsidence of pain while the treatment is being applied but the effect is not lasting. On the other hand if the part has been properly and adequately immobilized until firm union occurs pain is not much of a factor so these modalities since they do no recognizable good may be dispensed with.

Properly applied active motion may bring about a quicker return to normal function than will any other method or combination of methods. To clarify our ideas a few definitions are necessary.

Occupational therapy (3) or better still functional occupational therapy implies physical activity prescribed and guided to bring about active motion in the joints under treatment it is given in increasing doses as the patient shows improvement. This form of therapy provides a medium of carefully graded exercises or activities for joints stiffened by immobilization and atrophy of muscles and improves venous and lymphatic circulation in the extremities. Since these results are accomplished by active motion the return to normal function is accelerated. The purpose

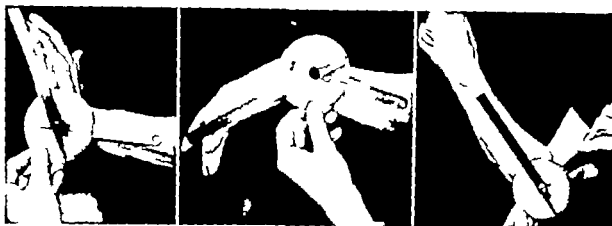


Fig. 1. Arthrometer used to measure subliminal motion of joint. (Courtesy Russell)

of the therapy is to arouse interest, courage, and confidence and to re-establish capacity for industrial usefulness (2). It should be supervised by the surgeon and directed to the correction of a particular need.

At Bellevue Hospital on the Fourth Surgical Division we have been using this form of treatment in fractures since 1927. This method on our division is used practically to the exclusion of all other methods. More recently we have not allowed the time before discharge of the patient from the hospital to go to waste. While the patient is still confined to bed, the occupational therapist comes to the ward and instructs the patient by various means of activities to move all joints and muscles of the extremity not actually encased in plaster or otherwise immobilized. When the patient is convalescent and about on crutches, he is sent to the occupational therapy in patient workshop for continuation and acceleration of this treatment. After discharge from the hospital the patient returns to the out patient department workshop three times a week and in the interim returns to the fracture clinic at intervals suggested by the surgeon. The occupational therapist also attends this clinic (with the patient's occupational therapy progress and joint measurement charts) to discuss with the surgeon and the patient the improvement noted and the increase of dosage indicated. In this way a complete progress record is kept.

The matter of records is very important and they must be kept accurately or they lose their value to both the surgeon and the pa-

tient (5). An arthrometer is used by the occupational therapist to measure the various joint. The instrument (Figs. 1, 2, 3) is simple to handle and easy to read. (A simple one can be made at home with two brass protractors and two sturdy brass or aluminum bars.) Each week the limitations of the joint motion are measured and recorded in graph form on the reverse side of the patient's progress chart. If the patient complains of joint pain and the measurement chart shows no progress or perhaps retardation, he is immediately referred back to the fracture clinic for further examination by the surgeon to discover what complicating factor is responsible for his lack of progress. When this trouble is corrected the therapy can again be resumed.

The specific application of activities as exercises is carefully worked out for all joints of the extremities and other supplementary activities such as dish washing, sweeping, etc. may be used or omitted as seems advisable in individual cases. All activities to be adaptable for exercises should have one or more of the following characteristics (6):

1. Repetition of the motion desired.
2. Gradation of the weights (that is, tools or equipment) or force (which could be the thickness or hardness of the wood or material) opposed to muscle action in proportion to its increase in strength.
3. The alternate contraction and relaxation of muscles.
4. Graded range of motion through which a joint is taken in performing any action.



Figs. 4 left and 5 center. Card board weaving device to promote flexion (Fig. 4) and extension of fingers (Fig. 5). Fig. 6, right. Winding material into ball. Ball is held in

uninjured hand while injured hand holds ball, promoting extension and flexion of fingers and adduction and abduction of wrist.

The treatment of fractures the aim of the occupational therapy is to assist in the restoration of joint motion and muscle strength and to induce voluntary motion by diversion of the mind (4). The frequency of treatment depends on the individual patient but usually it is given every other day by a trained occupational therapist and on intervening days home exercises are given to continue the active motion. Treatment is never carried beyond the fatigue point. In the beginning the activity period is short with rest periods between but as progress is made the activity periods are lengthened and the rest periods shortened. In fractures about the wrist such as a Colles fracture after the period of immobilization is over and the patient is examined by the surgeon in the fracture clinic it is customary immediately to refer him to the occupational therapy workshop for active motion. Usually he lacks grasp of fingers flexion and extension of wrist and pronation and supination of the forearm. The procedure of the occupational therapy treatment is carried out depending on the individual patient and his outstanding limitations and disabilities, approximately as follows:

Fingers principal disability—grasp

Simple card board weaving

1 Patient seated sideways resting injured fore arm on table (this to prevent added strain on arm). Hand pronated on loom patient actively attempts to flex fingers by pulling down on weaving threads (Fig. 4).

2 Loom reversed weaving threads are pushed into place by patient actively attempting to extend fingers (Fig. 5).

3 Adduction and abduction of thumb may be obtained by patient pushing threads into place with thumb.

Looping weaving material

1 Cloth cut into suitable width strips for weaving is slit at both ends. Patient (arm still resting on the table) is directed to loop each strip through the slits and thus make a continuous cord. Definite flexion of the fingers is required to do this. At first assistance may be given with the uninjured hand gradually doing more and more with the injured hand (Fig. 3).

Winding weaving materials

1 The aforementioned yards of cord are wound into balls. The size of the ball used depends on the limitation of the fingers (Fig. 6).

2 Winding is done with the uninjured hand and the ball is held in the injured hand (arm resting on the table). Fingers are extended and flexed and thumb adducted and abducted individually to allow strand to encircle ball.

Note: Activities are given for a limited number of times (say 5 with rest periods). As soon as the patient can perform a given activity with comparative ease he is advanced to a more difficult one.

Wrist principal disabilities—flexion extension pronation and supination

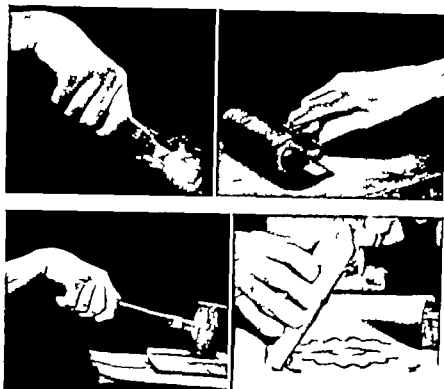
Block printing

1 Flexion of fingers—grasping brayer (roller) (Figs. 7-8).

2 Patient passes brayer back and forth over block printing ink (preferably water soluble) hand in pronation the backs and motion encourages flexion of wrist, the forward motion extension of wrist.

Note: Elbow is kept as quiet as possible but some compensation must be allowed with early fracture cases or patient might exert too much force against injured area which could result in damage to the bone or soft tissue. No attempt is ever made forcibly to hold the elbow forearm quiet.

3 The inked brayer is then lifted to the block (the size of block depending on patient's grasp) and the brayer rolled back and forth as described.



Figs. 7, 8 above, 9, and 10, below. Block printing, to promote flexion of fingers, pronation of hand, flexion and extension of wrist. Hammer tapping printing block promotes pronation of hand, hyperextension of wrist as well as flexion of wrist. Figure 10 shows print made.

4. Block is then raised on edge with uninjured hand (to prevent patient from smearing paint over himself) and lifted by the edges with extended fingers of injured hand and placed on paper to be printed. Slight supination is afforded in this process.

5. The block is tapped with a light weight hammer or mallet (usually 2 or 3 begin with) (Fig. 9). Hand pronated, the wrist is hyperextended as far as comfortable without forcing and the patient allows the weight of the hammer to flex the wrist when striking the block. No force is required or allowed in this procedure. The motion must all originate in the wrist itself or it is of no value. If the first print on the paper is not too distinct, it is of no importance, as each additional print will improve. Frequently the first print is kept to show the patient later and let him compare his improvement (Fig. 10).

6. Lifting the block with the injured hand from the paper and replacing it right side up on the table provide considerable supination.

7. Pronation and supination may also be obtained by use of hammer in tapping block for print. Holding the forearm in mid-position and tapping block first by supinating arm as far as possible without forcing, and then pronating arm as far as possible, without forcing (Fig. 11).

8. Adduction and abduction of wrist can be obtained by holding forearm in mid-position first

adducting and then abducting wrist when tapping block.

9. Gradation is obtained by gradually increasing the weight of the hammers 2, 5, 7 ounces increasing or decreasing the size of the block, according to limitations of flexion or extension gradually increasing the length of work periods.

Wood filing (circular stool top, breadboard, tray etc.)

1. Wood placed on end in vise

2. File held at both ends, with both hands (grasp) passed back and forth over circular surface. Extension of wrist is obtained as file moves forward. Flexion of wrist as file moves back (Figs. 12, 13).

3. This procedure may also be used with deep sanding block.

Sawing (use of small hand coping saw)

1. The wood used is 1 1/2 in. straight line to teach patient feel of the wood so that he will not be discouraged.

Holding saw handle (grasp)

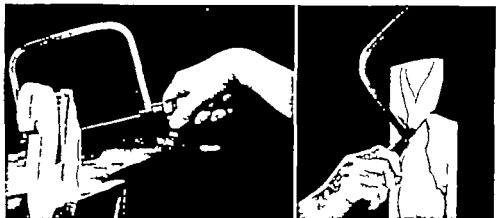
2. Hand in pronation, passing saw back and forth over wood, backward motion gives flexion of wrist, forward motion gives extension of wrist (Figs. 13, 14).

3. Supination may be obtained by turning saw upside down, and sawing up.

4. Gradation accomplished by increasing thickness and weight of wood.



Figs. 11, left and 12. Wood filling to promote extension as well as flexion of wrist.



Figs. 13, left and 14. Coping saw to promote flexion and extension of wrist as well as flexion of fingers in grasping saw handle

Screwing

1 Pronation and supination may be obtained by use of the screwdriver in the construction of a project (Care being taken not to use shoulder rotators)

Table I gives statistics showing the final results with various types of fractures (over a period of 5 years) in the out patient department workshop at Bellevue Hospital. Only fracture cases have been listed. The shop handles aside from this type of trauma, other cases such as burns severed tendons etc.

It has been the policy of the occupational therapy department to try to have the patient make three projects during his total treatment period. One of these he keeps for himself, the other two are sold by the department. The proceeds of these sales form a revolving fund which in turn purchases new materials, thus helping to defray the expenses naturally encountered in such an undertaking.

CONCLUSIONS

1 Occupational functional therapy is a distinct help in the treatment of injuries to the extremities. It rehabilitates the patient in the shortest possible time.

2 By means of the arthrometer and proper charting, progress becomes an accurate measurement rather than a guess.

3 Treatment is continuous and is carried out at the occupational clinic and at home.

4 Return to normal function is shortened in fractures of the extremities.

5 An accurate chart of all joint ranges is appended.

JOINT RANGES

No joint motion goes beyond 225 degrees. When measuring joint see this circle. Center of circle represents the joint. Above this is the immovable bone. This bone goes from center of circle to 0. Movable bone—from center of circle down.

TABLE I.—SUMMARIES
WRIST FRACTURES—246 Cases

Resurvey classification	No. of patients	Period of time spent in O.T.	Average total treatments	Those having less than treatment	Patients who returned to work
not		most days	19		3
Improved		most days			
Slightly improved		most days			
Unimproved		one to six days	3		
Did not return					
Not measured					
Total surveyed	25	most within 3 days		2	27

ELBOW FRACTURES—69 Cases†

		most 6 days	14		6
Improved	5	most 6 days			
Slightly improved	19	most six days			
Unimproved		most weeks			
Did not return	24				
Not measured					
Total surveyed	69	most six days		20	

SHOULDER FRACTURES—43 Cases

		3 most 5 days			
Improved	69	most six days		2	
Slightly improved	5	most six days	20		
Unimproved					
Did not return	5				
Not measured					
Total surveyed	43	most six days		20	33

KNEE FRACTURES—86 Cases

		most six days	14		
Improved		most six days			
Slightly improved		most six days			
Unimproved		most six days			
Did not return	6				
Not measured					
Total surveyed	86	most six days			

O. T. Occupational therapy.

* compensation—reversed fracture—surgical operation.
† open reduction—compensation case—psychopathic case—refused to cooperate.

not% Patients having both normal flexion and extension.

Improved Patients having normal motion in either flexion or extension but lacking 5 to 30 degrees in either direction; and patients lacking 5 to 30 degrees flexion or extension or both.

Slightly improved Patients having normal motion in either flexion or extension but lacking 35 to 90 degrees in either direction; and patients lacking 35 to 90 degrees flexion or extension or both.

Unimproved Patients having normal motion in either flexion or extension but lacking 95 to 99 degrees in either direction; and patients lacking 5 to 9 degrees flexion or extension or both.

Did not return Patients who reported for only one treatment.

Not measured Patients who reported for only one treatment and whom we were unable to measure at periods they reported.

Elbow joint Moves from 180 to 40 degrees. Normal range flexes to 40 degrees extends to 180 degrees range of motion—140 degrees

Fingers First joint—metacarpophalangeal joint flexes to 90 degrees, extends to 180 degrees range—90 degrees. Second joint flexes to 70 degrees, extends to 180 degrees range—110 degrees. End joint (distal phalanx) flexes to 140 degrees extends to 180 degrees range—40 degrees

Thumb Only 2 joints. Carpal metacarpal joint (in the hand) flexes to 120 degrees extends to 180 degrees range—60 degrees. Metacarpal phalangeal flexes to 160 degrees extends to 180 degrees. Range—20 degrees. Interphalangeal joint flexes to 90 degrees extends to 180 degrees range—90 degrees

Wrist joint Flexes to 100 degrees hyperextends to 245 degrees range—145 degrees

Shoulder joint Flexes to 70 degrees hyperextends to 220 degrees range—200 degrees

Ankle joint Measured from 180 degrees extension toward 0 decreasing the angle angle 115 to 170 degrees

Knee joint Flexes to 45 degrees extends to 180 degrees range—135 degrees

Hip joint Flexes to 60 degrees hyperextends to 220 degrees range—160 degrees

Degrees of abduction and adduction

Wrist Abducts to 155 degrees adducts to 215 degrees range—60 degrees

Shoulder abducts to 20 degrees adducts to 180 degrees range—160 degrees

Hip abducts to 115 degrees adducts to 180 degrees range—65 degrees

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SURGICAL TREATMENT OF URINARY OBSTRUCTION IN ARMY GENERAL HOSPITALS

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IN civilian practice urinary obstruction implies primarily diseases of the prostate. In the Army urinary obstruction presents a generous variety of lesions involving the entire urinary tract including an occasional obstructive prostate in the senior age group.

The obstructive lesions most frequently encountered in the Service are: (1) contractures of the bladder neck; (2) ureteropelvic constrictions with or without aberrant renal vesicles; (3) urethral strictures and small meatuses. These obstructions are seen somewhat earlier in the Army than in civilian patients because the advanced cases are screened out by induction urine examinations. At least 90 per cent of these obstructions probably existed prior to induction. Service-connected aggravation may result at any time by interposing infection or calculi or both.

The purpose of this paper is to point out that after careful evaluation it is possible to correct many of these obstructions and restore these patients to full military duty.

CONTRACTURES OF THE VESICAL NECK

Narrowing of the bladder outlet due to fibrosis or muscular hypertrophy is a common lesion seen in an Army general hospital. Many of these obstructions manifest themselves during early childhood and adolescence. They are slowly progressive. Contractures may be classified as mild, moderate, and severe. They can be separated clinically into 3 groups depending upon the degree of progression. Group I: Stage of vesical irritation manifested by intermittent frequency, urgency, or nocturia with a clear urine. Group II: Stage of residual urine and trabeculated bladder. During this period there is a noticeable narrowing of

the urinary stream with difficulty in voiding. Sexual symptoms as premature ejaculations, desire to masturbate, or sexual neurasthenia may also plague these patients. During acute exacerbations urinary symptoms become more severe, often associated with terminal dribbling, dysuria, suprapubic and perineal discomfort, backache, renal colic, or hematuria. Group III: Stage of acute retention of urine with inability to void.

Pathologically these contractures may be divided into superficial and deep. In the former there is a superficial bladder neck sclerosis without adnexal involvement. In this superficial group we also find the pure bladder neck muscular hypertrophy producing urinary obstruction (Fig. 1). In the latter group the bladder neck fibroses result from long standing associated chronic posterior urethritis and prostatovesiculitis. A well established fibrosis will result either in shortening of the retromontane urethra or the trigone of which urethral shortening is more common in the ratio of 5 to 1. Bladder deformities, diverticula, pyelonephritis, and infected hydronephroses are associated pathology noted in advanced infected cases. Multiple diverticula are more apt to develop in the presence of inflammatory bladder neck obstructions.

The diagnoses are made from the history and physical findings. The latter may be entirely negative. Cystourethrograms reveal vesical neck constriction and the associated bladder pathology. Rectal palpation of the bladder neck over an instrument in the deep urethra will reveal the degree of posterior commissural thickening. Cystoscopy shows the deep urethral vesical neck, trigonal and bladder wall changes. Elevation of the posterior vesical lip with deformity of the vesical outlet is readily observed.

The treatment of the early cases should be conservative. Bedrest, sedatives, and heat

From the Genito-Urinary Subsection of the Surgical Service, Bushnell General Hospital, Brigham City, Utah.
Read before the Utah State Medical Association, Salt Lake City, Utah, August 26, 1944.



Fig 1 Med. Officer age 42 years. Smooth muscle hypertrophy of vesical outlet resulting in 900 cubic centimeters of infected residual urine and bladder atony. Six grams of tissue removed successfully transurethraly. Duty.



Fig 2 Age 38 years. Marked fibrosis of vesical neck and prostatic calculi. Diffuse *Staphylococcus aureus* urinary tract infection. Sulfonamides and penicillin resistant. Improved following transurethral resection of 20 grams of tissue.

will improve the symptoms. Urinary anti-septics are rarely helpful. Bladder neck dilatation may temporarily relieve the symptoms and suggest early contracture. When symptoms of vesical irritability are temporarily relieved following cystoscopic examination a contracture should be suspected. After these patients have reached the stage of residual urine or acute retention transurethral resection is indicated. Surgery in these cases may accomplish more than years of prostatic massage and local treatment. It is necessary to remove 5 to 20 grams (Fig 2) of obstructive tissue from the bladder neck, posterior urethra and prostate for satisfactory postoperative bladder drainage. Carefully selected patients operated upon can be rehabilitated and returned to full duty after 8 to 12 weeks' hospitalization. Neurogenic bladders associated with a mild vesical neck obstruction lend themselves equally well to bladder neck resection and improved bladder function. A mild bladder neck obstruction becomes a major obstruction in the presence of a weakened detrusor muscle.

HYDRONEPHROSIS

The most common lesions of the upper ureter interfering with free renal drainage are ureteropelvic strictures, aberrant lower pole renal vessels, periureteral adhesions and kinks

The presence of a calculus or calculi will further impede renal drainage. Occasionally postoperative peripelvic and periurethral fibroses will develop and cause obstruction. Ureteral strictures and aberrant vessels are noted clinically more frequently in the second decade. They are congenital and are usually asymptomatic until infection or calculi or both have developed. They may be unilateral or bilateral. In degree they are mild, moderate or severe. After infections develop these kidneys are resistant to conservative treatments including the sulfonamides and penicillin. These therapeutic agents may temporarily clear the urine, but relapses are the rule. Intravenous and retrograde pyelograms, bacterial and renal function studies will usually suffice for accurate diagnoses.

The treatment of these lesions is primarily surgical. In a few instances temporary improvement may result following ureteral dilatation. The surgical correction consists of pyeloplasties on the ureteropelvic junction, resection of aberrant vessels, resection of large pelvises and nephropexies. We favor the Heineke-Mikulicz and the Foley Y-plastic procedures. The preferred plastic procedure in most cases is best determined at the operating table. The best functional results are obtained when surgical correction is undertaken prior to infection. Preoperative and post-

operative sulfonamides or penicillin or both will greatly enhance satisfactory surgical results. Infected pyeloplasties should be splinted with a small soft rubber catheter or a common duct T tube as recommended by Deming. Uninfected pyeloplasties followed by renal fixation do not need ureteral splinting. In fact ureteral splinting may invite postoperative infection. When the pelvis is large partial resection will aid postoperative renal drainage (Fig 3). In advanced cases temporary pyelotomy or nephrostomy drainage tubes should be utilized.

Aberrant renal vessels may be treated by resection or reimplantation of the ureter. When only a small amount of renal parenchyma is involved removal of the vessel or vessels is the operation of choice. The extent of the aberrant arterial blood supply can be quickly determined by simple compression of the vessel. Coexisting ureteropelvic narrowing can be easily overlooked at the time of operation. In some instances better results could be obtained if a pyeloplasty were done in addition to removal of the vessels (Fig 4). All patients operated upon should have follow up postoperative excretory pyelographic studies so that the final result may be evaluated.

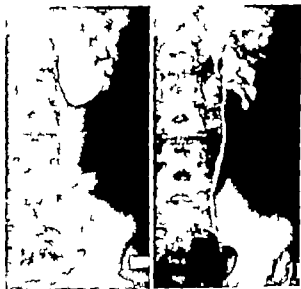


Fig 3. Age 30 years. Stricture of ureteropelvic junction, hydronephrosis, calculi (). Pyeloplasty and pelvic resection. Postoperative pyelograms revealed satisfactory result. Duty.



Fig 4. Age 30 years. Aberrant artery and vein, ureteropelvic kink and adhesions, and infected hydronephrosis. Resection of aberrant vessels and release of adhesions. Improvement, questionable mild postoperative pelvic retention. Duty.

URETHRAL STRICTURES

Urethral strictures small and wide caliber were noted in 12 per cent of our admissions. The wide caliber (larger than 20 F) except for producing a slight morning drop a mild pyuria and shreds in the first glass of urine may be asymptomatic. They frequently respond promptly to one or two urethral dilations. Asymptomatic large caliber fibrous strictures should be left alone. The small caliber multiple anterior urethral strictures present a complex military therapy problem. They occur more often in a soldier who has had repeated gonorrheal infections and recurrent urethral discharges. Examination reveals a purulent discharge, pyuria, adnexitis, with or without chronic epididymitis. When severe strictures are complicated with acute gonorrhea and/or trichomonas genitalis the latter are usually resistant to sulfonamides and penicillin. Improvement in urethral drainage is the keynote in their management. This may be accomplished by progressive urethral dilatation or internal urethrotomy. Symptomatic urethral strictures should be treated by progressive dilatation. Fibrous and resilient



Fig 5. Age 37 years. Neuromuscular deficiency and left renal calculi. Exploratory and ureteral mobilization was followed by increased ureterectasis due to inadequate intrinsic innervation. Certificate of Disability Discharge.

strictures respond poorly to dilatation. These resistant strictures should be cut. In our hands electrourethrotomy gives superior results. Severe urethral strictures necessitate long hospitalization, observation and treatment. With notable exceptions the severe anatomical and physical disabilities preclude probable military rehabilitation. Before treatment is undertaken, separation from the service should be considered particularly in the maladjusted individual. Service-connected urethral injuries and strictures, however, should receive every consideration of current available therapeutic measures.

Small external urinary meatuses are usually congenital and have no clinical significance except in the presence of urethritis. Improved urethral drainage by simple meatotomy will aid materially in clearing some patients with resistant venereal or nonvenereal urethritis.

CASE 1. J. E. B., aged 21 years, acquired gonorrhea overseas 2 months before. He received 125 grams of oral sulfonamides and 4 courses of penicillin total 700,000 units while overseas, without benefit. Smear and culture on admission June 17, 1944, were positive for gonococci. Examination revealed a redundant prepuce, small meatus, purulent discharge and hazy urine. Circumcision and meatotomy were carried out 3 days later. Subsequent smears and cultures remained negative. Provo-

cations failed to reactivate the disease. Considered clinically well July 13, 1944.

INTRINSIC URETERAL STRICTURES

Intravenous pyelography more than any other diagnostic procedure has helped to suspect and identify ureteral strictures. The incidence is approximately 2 per cent in large series of urologic examinations. Ureteral strictures are relatively asymptomatic until sufficient obstruction develops to invite infection. Suspected ureteral strictures can be verified by ureteral calibration. However, our interpretation of ureteral blockage to a catheter can be very misleading. Nonopaque calculi, mucosal pockets, lateral angulation and spasm are frequently erroneously diagnosed as strictures. Neuromuscular deficiencies (Fig 5) and ureteral dilatation resulting from chronic infection frequently suggest stricture on pyelography (Fig 6). In these cases ureteral calibration will usually rule out intrinsic strictures. The treatment of ureteral strictures is progressive dilatation and clearing of the coexisting infection. Extrinsic ure-



Fig 6. Age 24 years. Pyelonephritis, bilateral, severe. *Staphylococcus aureus*, temporarily improved with penicillin. Bilateral ureterectasis due to chronic infection. No 9 F catheters passed easily. Iregnolds poor. Certificate of Disability Discharge.

teral lesions causing urinary obstruction are omitted from this discussion

OBSERVATIONS

The problem of urinary obstruction in the Army presents the same overall picture as seen in civilian practice. When dealing with large numbers of young men, congenital obstructive lesions predominate over the acquired obstructive lesions of senescence. Many obstructive lesions in the Army are noted before serious complications have had the opportunity to develop. Army Medical Officers following the slightest suspicion of obstructive pathology carry out urologic examinations sufficiently early to turn up many of these serious developing lesions. The earlier these cases are accurately diagnosed the more amenable they are to correction. Surgical reconstruction of the pelvic or bladder outlet obviously is simpler in early uninfected cases than in late neglected ones.

Surgeons of experience are alert to the tremendous opportunities in conservative renal and bladder surgery. Aside from some anatomical landmarks it does not require an unusual amount of surgical skill to remove a kidney. On the other hand conservative renal surgery is not unusually difficult either. It does require however a surgeon of sufficient experience who is anxious to restore as well as remove. In addition carefully trained and organized personnel and equipment are essential to achieve the best results. The activation of Army Surgical Centers during this emergency by the Surgeon General has aided immeasurably in the rehabilitation

of patients requiring highly specialized treatments.

In the Army then there is ample opportunity to apply principles of recognized urologic conservative measures. These applied procedures will not only rehabilitate these patients during this emergency, but will in a great measure add to their health and happiness following their discharge from the service.

It has been charged that the Army neglects to take care of some of these FPTI (existed prior to induction) lesions. This charge may well be true. A surgeon in the Army however must evaluate the entire individual, his length of service as well as the specific lesion in question. Surgery performed upon an unhabilitated soldier may facilitate later pension claims to our government from \$30,000 to \$50,000 each.

CONCLUSIONS

1. Urinary obstruction in the Army is a common lesion involving most frequently the upper ureter, bladder neck and urethra.

2. The majority of these lesions existed prior to induction.

3. The prostatic diseases of senescence are uncommon.

4. Ample opportunity exists in the Army to correct these congenital obstructive lesions early with minimum morbidity and mortality.

5. In maladjusted and inadequate Service patients surgery for lesions which existed prior to induction unless emergent is usually contraindicated.

REFERENCE

DRIVING C. or I. J. Urol. Bull. 44:3 50-4

ANATOMICAL AND SURGICAL RESTUDY OF DENONVILLIERS FASCIA

CHARLES E. TOBIN Ph D and JOHN A BENJAMIN M D Rochester New York

THE tissue which lies anterior to the rectum and posterior to the prostate seminal vesicles and bladder has become known as the fascia of Denonvilliers (Fig 1) from his description of this tissue in 1836 and 1837. Since the present interpretation of the position and structure of this tissue appears to be uncertain Denonvilliers' description of this fascia (Fig 2) and its translation are given as the first step in the approach to this restudy.

Behind the prostate, between the seminal vesicles and the rectum, there is a distinct membranous layer which I call prostatoperitoneal. This is its position from the two sides it fuses with the compact cellular tissue which surrounds the venous plexus at the base of the bladder on the anterior side it loses itself in the most distant side of the prostate on the posterior side it adheres to that part of the peritoneum which descends between the bladder and the rectum. This adherence, very marked, as close as if it were fused with the tissue, explains the constancy of the rectovesical cul-de-sac of the peritoneum the half-moon form of this cul-de-sac which lies at the posterior border of the aponeurosis that always describes a curve with convexity in front, or which represents (as in the form of a V) jutting in anteriorly at an angle. The inferior surface which touches the rectum barely adheres to it by a very loose cellular tissue from the upper surface however some thick cellular projections arise which surround the seminal vesicles. The texture of this membranous layer resembles that of the dartos. It appears to be formed principally by fibers which separate while radiating from the posterior part and those occupying the median line are the most prominent. In vigorous subjects some evident muscular fibers exist, but only on the sides. Whatever is the additional arrangement of this membranous layer it is very resistant, and forms a completely closed space at the base of the bladder, in which the seminal vesicles and a part of the ureters and vasa deferentia are enclosed these enter into the cavity by means of very thick cellular tissue which forms their lateral sides.

Subsequent to Denonvilliers' description of the prostatoperitoneal membrane many conflicting reports have been published as to its embryological origin gross anatomical structure and surgical importance. Two diametrically opposed embryological theories have been advanced Cuneo and Veau (1899)

Smith (1908) and others claimed that all of this tissue is derived from a cul-de sac of peritoneum which extends into the pelvis of the fetus and young individual. On the contrary Wesson (1922 and 1923) maintained that Denonvilliers' fascia is derived from the mesenchyme around the rectum prostate seminal vesicles and bladder and that the cul-de sac of pelvic peritoneum between these structures reverted to undifferentiated embryonic tissue or persisted for a short time as a pseudoraphe or wherever apposition had not been complete a cyst may form.

The gross anatomical structure of the prostatoperitoneal membrane has been described as consisting of one or more layers depending on the interpretation of the original description of this tissue and the cleavage planes made in dissecting this region. Descriptions have been given of (1) a layer of areolar tissue surrounding the rectum which might contain a considerable amount of fat in some individuals (2) a resistant glistening layer forming the posterior covering of the seminal vesicles and prostate (3) a continuation of this resistant layer over the anterior surface of the seminal vesicles (between the bladder and seminal vesicles) (4) a V shaped fibrous membrane extending from the urogenital diaphragm to the peritoneum which is adjacent to or fused with the posterior layer of the prostate and seminal vesicles and (5) a similar band attached to the connective tissue on the superior border of the seminal vesicles (Denonvilliers 1836 and 1837 Smith 1908 Wesson 1922 and 1923 Young 1926 Hinman 1935 Belt and associates 1939 Lowsley and associates 1942 and others).

Clinically Denonvilliers' fascia is not only an important anatomic landmark in the surgical approach to the prostate and seminal vesicles but it is also considered an effective barrier in limiting the spread of pus extravasated urine and malignant tumor of the prostate

From the Department of Anatomy and Department of Surgery Division of Urology The University of Rochester School of Medicine and Dentistry.

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REFERENCE

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perineal vesicles and rectum. Therefore the following study was undertaken as an attempt to clarify the embryological origin and anatomical structure of Denonvilliers' fascia and to ascertain the part of the fascia entered in the perineal approach to the prostate.

MATERIAL AND METHODS

Sections from 11 human embryos (6 mm CRL to full term) were studied for the embryological development of Denonvilliers fascia. Seven of these embryos were from our embryological collection and the other four embryos from the Department of Embryology, The Carnegie Institution of Washington, Baltimore, Maryland. Additional studies were made on dissected pelvises of a 7, 8 and 9 month fetus and 2 newborn infants.

The composition and extent of this fascia in the adult were ascertained by a study of (1) Four specimens in which the anterior wall of the rectum the posterior part of bladder and

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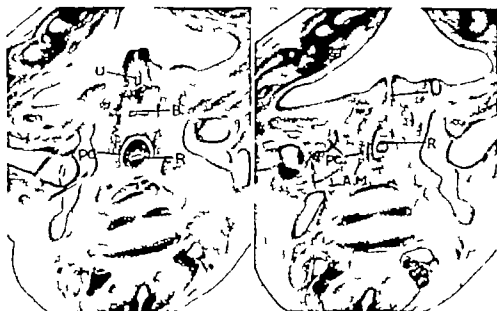


Fig. 3 left. Photomicrograph of a transverse section through the pelvis of a 19.5 millimeter human embryo. Both developing rectum *R* and bladder *B* are surrounded by mesenchyme. The peritoneal cavity, *PC* intervenes between these layers of mesenchyme and surrounds three sides of the developing rectum. The position of the urethra, *U*, is shown. (U of R. Embryo No. 30 slide 57 row 4, section 3.) $\times 14$.

Fig. 4. Photomicrograph of a more caudal, transverse section of the embryo shown in Figure 3. The peritoneal cavity *PC* extends caudally to the level of the developing levator ani muscles, *L.A.M.*, at the lower end of the rectum *R*. This section is below the level of the bladder. The course of the urethra, *U* is shown. (U of R. Embryo No. 30 slide 58, row 3 section 6) $\times 14$.

ing these layers. The composition of the glistening layer over the posterior surface of the prostate was determined by similar histological sections from biopsy of this tissue during perineal prostatectomy in the living.

ANATOMY OF DENONVILLIERS FASCIA

A Embryology. The rectum pelvic urogenital organs and their connective tissues were not differentiated sufficiently in the three younger embryos studied (6.65 and 7.7 mm C.R.L.) to determine the tissues that would form the future Denonvilliers fascia. The peritoneal cavity in these embryos however was observed to extend caudally to the developing pelvic floor.

More advanced differentiation of the pelvic organs and the anlage of Denonvilliers fascia were found in older embryos (16.5, 19.5, 26.58, 67, 70, 140 and 161.4 mm C.R.L.). In these specimens three layers of tissue were present between the rectum and pelvic urogenital organs: (1) a layer of mesenchyme surrounding the epithelium at the site of the developing bladder seminal vesicles and

prostate; (2) another layer of mesenchyme around the developing rectum; and (3) between these two layers of mesenchyme the pelvic continuation of the peritoneal cavity consisting of a mesothelium lined sac surrounded by a thin layer of subjacent mesenchyme. The pelvic cul-de-sac of peritoneum extended caudally to the pelvic floor and laterally around the sides of the rectum in younger embryos (Figs. 3 and 4). In older embryos the mesenchyme from the cul-de-sac of peritoneum was found behind the developing seminal vesicles and prostate (Figs. 6 and 7).

The mesenchyme surrounding the pelvic urogenital organs and rectum differentiated primarily into the musculature and connective tissue associated with the epithelial lining of these structures in older embryos (Figs. 8 and 9).

Our attention will be focused particularly on the connective tissue derivatives of this mesenchyme and that part of the peritoneal cul-de-sac which becomes associated with this connective tissue to form Denonvilliers fascia in the adult.

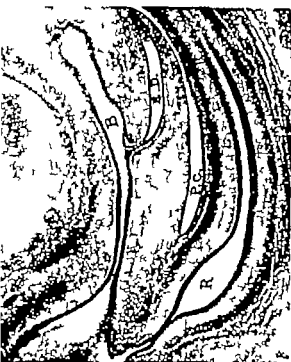


Fig. 5. Sagittal section through pelvis of 26 millimeter embryo showing mesenchyme around bladder B, ejaculatory duct, E, D, and rectum R. Peritoneal cavity P, C, extends between structures, lower part is becoming obliterated. Cyst like areas remain where mesothelial surfaces have not fused. (Carnegie Inst. Embryo 43 slide 2, row sec.) X44



Fig. 6, left. Photomicrograph of sagittal section through pelvis of 67 millimeter human embryo. In this specimen, the developing prostate, P, and seminal vesicles, S, are imbedded in layer of connective tissue. The peritoneal cavity, P, C, extends between the rectum, R, and the vas deferens, V, and seminal vesicles. The caudal end of the peritoneal cavity between the prostate and rectum, has been obliterated and consists only of layer of connective tissue. The position of the symphysis pubis, S, and urethra, U, are indicated. (Carnegie Inst. Embryo No. 656, slide 48.) X 2.

With growth and change in position as well as functional distention of the pelvic viscera the caudal end of this cul-de-sac of peritoneum was progressively obliterated by approximation and fusion of the two mesothelial surfaces. Cyst like areas of mesothelium remained where fusion of these surfaces was not complete (Fig. 5). It is apparent therefore that the peritoneal cavity did not extend as an open sac as far as the pelvic floor in older embryos. In the younger embryos of this study the levels of fusion of the peritoneal surfaces were the same as those given by Wesson (1922). However whereas he stated that the peritoneum only extends to the middle of the seminal vesicles in the 240 millimeter embryo we found that the peritoneum covered the posterior surface of the prostate at this age and in older embryos (Fig. 12).

The mesenchyme originally subjacent to the mesothelial surfaces remained and differentiated into a fibrous membrane. This membrane had the same relation to the connective tissue around the rectum and pelvic urogenital organs as the original layers of the cul-de-sac of peritoneum. The development of this fibrous layer could be demonstrated in sections from the embryos of various ages.



Fig. 7. Photomicrograph of more lateral section from embryo shows in Figure 6. Note that the peritoneal cavity, P, C, in this section does not extend between the seminal vesicles, S, F, and rectum, R, but connective tissue, derived mainly from the peritoneum, is found between these structures. Other labels are the same as in Figure 6. (Carnegie Inst. Embryo No. 656, slide 49.) X 2.

In young embryos the peritoneum covered the entire posterior surface of the seminal vesicles, apparently due to the lateral growth and increase in the transverse diameter of the pelvis and peritoneal cavity. With increasing age the peritoneum here like that posterior to the prostate underwent the same changes and formed a fibrous membrane (Fig 7).

In all the embryos studied the pelvic peritoneum covered only the posterior surface of the prostate and was not found to extend around its sides or anterior surface. In describing the tissue in these locations Denonvilliers must have had in mind connective tissue derived from mesenchyme which surrounded the prostate and became adherent to the sides of the prostatoperitoneal membrane since this membrane covered only the posterior surface of the prostate. However the pelvic cul-de-sac of peritoneum did surround three sides of the developing rectum being absent only along its sacral border (Fig 3).



Fig. 8, left. Photomicrograph of a transverse section through prostate and rectum of 140 millimeter human embryo. The peritoneal cavity *P.C.* extends between rectum *R* and lower part of the prostate *P*, shown by this level cut through the verumontanum *V* and ejaculatory ducts, *F.D.* The musculature and connective tissue around the prostate and rectum are differentiated. (U. of R. Embryo No. 183 slide 3 row 1 section 3.) $\times 16$

A similar cul-de-sac of peritoneum extended between the rectum and uterus in developing female embryos (Fig 10). The homologue of Denonvilliers fascia in the adult female will be described in a separate report.

B Infant In the full term fetus or new born infant (Figs 11 and 12) the connective tissues surrounding the prostate and rectum were differentiated but were not as dense as those of the adult. The peritoneal cul-de-sac was closed more cephalad due to pressure on it from the growth and distention of the pelvic organs anteriorly and posteriorly. With cephalolateral growth of the seminal vesicles the peritoneum may extend for a short distance between the bladder and seminal vesicles (Fig 12). The fibrous membrane remaining from the fused portion of the cul-de-sac of pelvic peritoneum extended from the pelvic floor to the peritoneum covering the pelvic

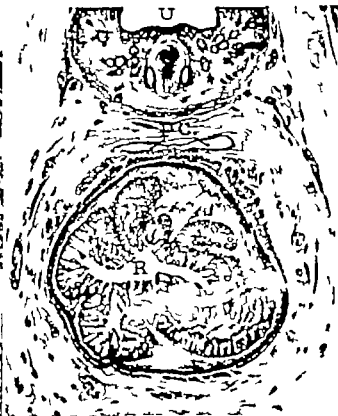


Fig. 9. Photomicrograph of a transverse section through the prostate and rectum of a 161.4 millimeter human embryo. The peritoneal cavity *P.C.* between the connective tissue around the rectum *R* and prostate *P*, partly obliterated and does not extend as far caudally as it is found to extend in the younger human embryos. *U* Urethra. (Carnegie Inst. Embryo No. 1049, slide 82 row 1 section 1.) $\times 14$.

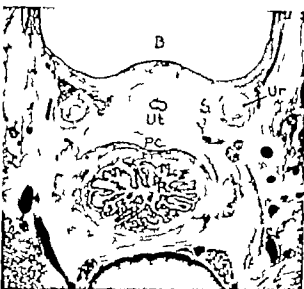


Fig. Photomicrograph of transverse section through the pelvis of 70 millimeter female human embryo. The peritoneal cavity PC extends between the connective tissue around the rectum R, and uterus, U, just as it is found between the prostate and rectum of the neonate. B Bladder U ureter (U of R. Embryo N 20, slide 2, row section 5) X 4.

viscera in most of the specimens. In one newborn infant the caudal end of the cul-de-sac was closed up to the middle of the prostate.

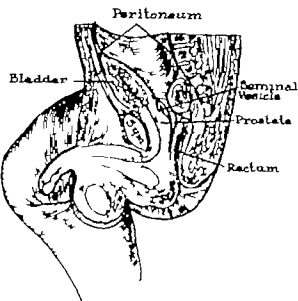


Fig. Drawing, median view from the pelvis of full term fetus. The pelvic cul-de-sac of peritoneum extends between the seminal vesicles, prostate and rectum and also between the upper part of the seminal vesicles and bladder $\frac{1}{2}$ normal size.



Fig. 1. Photomicrograph of a transverse section through the pelvis of full term fetus. The layers of Denonvilliers' fascia, D, are formed by the connective tissue around the rectum, R, and prostate, P, and that from the obliterated cul-de-sac of pelvic peritoneum. Note relation of levatores and muscles, LAM, to rectum and prostate. (Carnegie Inst. Embryo N 2400, slide 99, section 5) X 6.

1. *Adult* Between the posterior surface of the seminal vesicles bladder and prostate and the anterior surface of the rectum the following tissues were encountered (1) A layer of rectal fascia (areolar or fatty tissue) was found immediately external to and mingled with the external longitudinal musculature of the rectum. The amount of adipose or areolar tissue in this fascia depended on the body type of the individual (Figs. 14, 15 and 16). Clinically this layer has been described as the posterior layer of Denonvilliers fascia. (2) Anterior to the connective tissue around the rectum there was a fibrous membrane the remains of the connective tissue from the cul-de-sac of peritoneum which extended from the pelvic floor to the peritoneum covering the cephalic surfaces of the pelvic organs. This fibrous membrane was very thin in some

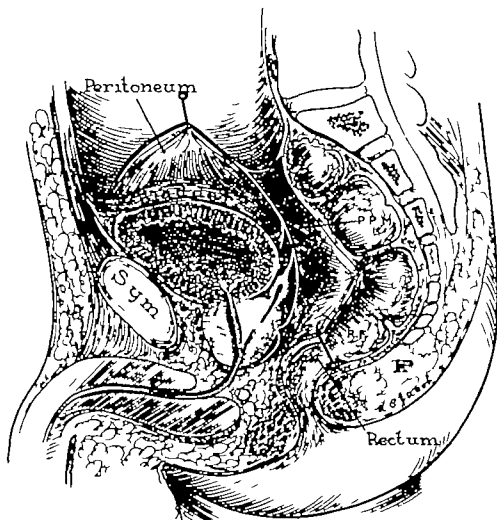


Fig. 13. Drawing of median view (right half) of adult male pelvis. The rectum and its fascia, *R.F.* have been retracted posteriorly. The peritoneum is retracted cephalad from the vertex of the bladder and the prostatoperitoneal membrane (anterior layer of Denonvilliers' fascia, *P.P.M.*) is retracted posteriorly from the prostate and seminal vesicles. This layer extended from the inferior surface of the prostate to the pelvic peritoneum. Fibrous bands extended from the membrane to the cephalic border of the seminal vesicles and to the bladder. The lateral parts of the membrane extend around the sides of and fuse with the rectal fascia. $\frac{1}{4}$ normal size.

specimens while in others it was quite thick. It usually had the form of a V as described by Denonvilliers (1836 and 1837). The apex of the V was attached to the superior layer of the urogenital diaphragm at the inferior border of the prostate and the two limbs of the V separated as they ascended dorsolaterad to cover the posterior surfaces of the seminal vesicles (Figs 13 15 20 21 and 22). At the junction of the ampullae and ejaculatory ducts to the prostate this fibrous membrane was fused to the prostatic capsule (Fig 20). The clinical importance of this fusion will be discussed. The connective tissue around the sides and front of the prostate

which was derived from mesenchyme surrounding the neck of the bladder adhered to the sides of the prostatoperitoneal membrane. Other fibrous sheets of similar structure and also differentiated from the cul-de-sac of peritoneum extended from the cephalic border of the seminal vesicles and posterosuperior surface of the bladder to the pelvic peritoneum (Figs 13 15 20 and 21).

This fibrous membrane extended laterally around the sides of the areolar or adipose tissue of the upper part of the rectum in the adult as lateral extensions of the arms of the V (Figs 13 21 and 22). The relation of the pelvic cul-de-sac of peritoneum in the embryo

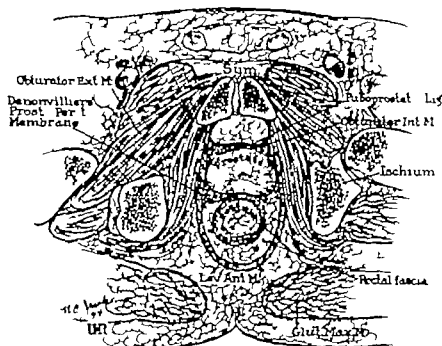


Fig. 4. Drawing from transverse section of adult male pelvis, cephalic (lea). This section shows the position of the rectal fascia (adipose and fibrous tissue) around the rectum, the relationship of the levator ani muscle to the rectum and prostate, and the position of the prostatic capsule. The prostatoperitoneal membrane (anterior layer of Denonvilliers' fascia) is fused to the prostatic capsule dorsal to the posterior lobe of the prostate. The retroperitoneal pad of fat anterior to the prostate is the space of Retzius. $\frac{1}{3}$ normal size.

which differentiated into this part of the fibrous membrane around the rectal tissue in the adult is shown in Figure 3.

The thickest part of this fibrous membrane was found over the posterior surface of the prostatic capsule. When well developed it was white and glistening in appearance. However, where it extended over the posterior surface of the seminal vesicles and laterally around the sides of the rectal fascia, this membrane was much thinner, more areolar than fibrous in structure, and grayish in color (Figs. 15, 16).

Denonvilliers described this membrane as being similar to the dartos and stated that it contained muscle fibers at its lateral sides in vigorous individuals. Histological sections taken from various regions of this membrane contained scattered bundles of smooth muscle fibers intermingled with the collagenous and elastic fibers of the membrane (Fig. 19). The embryological origin and the functional and clinical significance of the smooth muscle in this membrane are not clear at present.

DISCUSSION

The two opposing views of the embryological origin of Denonvilliers' fascia, i.e., entirely from mesenchyme (Wesson, 1922 and 1923) or entirely from parts of the pelvic portion of the peritoneum (Cunéo and Veau, 1899; Smith, 1908, and others) appear to be due to the differences in the concept of the tissues making up the peritoneum. In the embryo as well as in the adult the peritoneum (as defined in the standard texts of histology) consists of a surface layer of mesothelial cells and a subjacent layer of mesenchyme or connective tissue which supports the mesothelial layer and contains the vessels and nerves of the peritoneum. As we have shown, the developing embryo has a connective tissue layer around the rectum, a similar layer around the prostate, seminal vesicles, and bladder. Between these two visceral layers there is a continuation of the peritoneum, composed of a mesothelium-lined cavity surrounded by a subjacent layer of connective tissue. Therefore, one encounters four layers

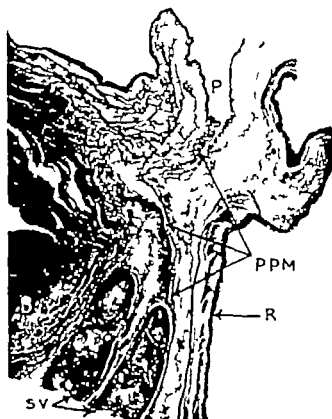


Fig. 5. Photomicrograph of a sagittal section from a block containing the anterior rectal wall, *R*, posterior part of the bladder *B*, upper part of the seminal vesicles, *S1*, and peritoneal cavity *P*. Note the continuation of the prostatoperitoneal membrane or anterior layer of Denonvilliers fascia, *P.P.M.*, indicated by arrows extending inferiorly from the peritoneum, *P*, to a point where it comes to lie posterior to the fibromuscular covering of the seminal vesicles. Between this membrane and the rectal musculature is a layer of areolar tissue, the rectal fascia. $\times 29$.

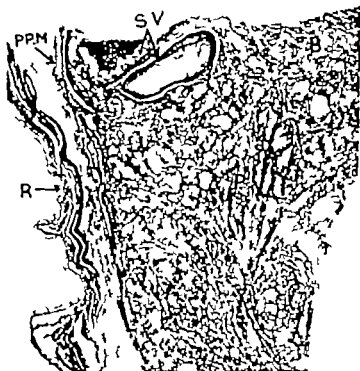


Fig. 16. Photomicrograph of a sagittal section from a block containing the anterior wall of the rectum *R*, prostate, *P*, base of the seminal vesicles, *S1*, and part of the bladder musculature, *B*. The prostatoperitoneal membrane or anterior layer of Denonvilliers fascia, *P.P.M.*, is thin and closely applied to the prostatic capsule but is separated from rectal musculature by areolar rectal fascia. Note continuation of fibromuscular tissue of prostate around and over base of seminal vesicles. The glandular epithelium of prostate is very near the prostatic capsule. $\times 417$.

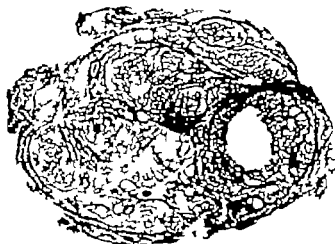


Fig. 7. Photomicrograph of prostatic tissue showing increase in amount of fibromuscular tissue on the surface and around the areas of benign prostatic hypertrophy (left side and lower right half of section). $\times 35$.



Fig. 8. Photomicrograph of prostatic tissue showing decrease or absence of fibromuscular tissue around the areas of cancer. Compare right and left parts of section and with Figure 7. $\times 35$.



Fig. 9. Photomicrograph of a section through the prostatoperitoneal membrane of Denonvilliers (anterior layer of Denonvilliers fascia) taken near the posterior inferior surface of the prostatic capsule. The bundles of smooth muscle are seen controlling the areolar tissue of this layer $\times 70$.

of connective tissue in the region of the developing Denonvilliers fascia—two layers associated with the viscera and two others one on each side of the mesothelium of the pelvic peritoneum. Depending on the concept one has of the layers of tissue making up the peritoneum, it can be understood readily how the mesenchyme remaining from the regression and disappearance of the mesothelial layers during closure of the peritoneal cul-de-sac could be interpreted as part of the mesenchyme around the viscera or all of the pelvic mesenchyme could be interpreted as part of the peritoneum. The fusion of the mesothelial surfaces of the cul-de-sac of peritoneum may be due partly to the change in position of the bladder as well as to its growth and functional distention. Dine (1892) described the descent of the bladder as being rapid during the first 3 years slower from the 4th to 9th years, with little change in position between that age and puberty after which the descent is renewed and the bladder gains its final position at the pelvic floor by the 21st year.

When two peritoneal surfaces are approximated in the embryo through change in posi-

tion of the viscera the mesothelial surfaces become adherent, retrogress, and disappear. The connective tissues associated with the mesothelial surfaces remain however as fibrous sheets. Toldt (1893) described this process for the peritoneal surfaces associated particularly with the intestine. According to our studies the pelvic cul-de-sac of peritoneum underwent similar changes. Furthermore a fold of peritoneum was found between the bladder and seminal vesicles during development of the pelvic organs (Fig. 12). This peritoneum was external to the fibromuscular covering of the seminal vesicles and in older specimens formed only a fibrous strand extending from the cephalic borders of the seminal vesicles and posterosuperior border of the bladder to the pelvic peritoneum. These studies also agree therefore with those of Smith (1908) and Cunéo and Veau (1899) who stated that the tissue between the bladder and seminal vesicles was derived from the peritoneum.

Our studies indicate that the only part of Denonvilliers fascia to be derived from peritoneum was the fibrous membrane remaining after obliteration of the cavity in the pelvic cul-de-sac of peritoneum. This membrane was located between the loose connective tissue around the rectum and the more dense fibromuscular connective tissue around the prostate and seminal vesicles. Contrary to Wesson's view that the peritoneum reverts to undifferentiated tissue in the embryo we found the fibrous membrane derived from the peritoneum to be present in all of the adult specimens and its origin could be traced in the variously aged embryos and fetuses studied. This membrane in the adult was nearer the prostate than the rectum—being close to and in certain areas adherent to the fibromuscular covering of the prostate. A layer of areolar or adipose tissue (rectal fascia) intervened between this membrane and the rectal musculature. If the mesothelial surfaces persist the cul-de-sac might remain open and form a direct connection with the peritoneal cavity. Herniation into a pelvic continuation of the pouch of Douglas is known to occur (Callander 1939). Cyst-like areas could be formed where the mesothelial surfaces remain be-

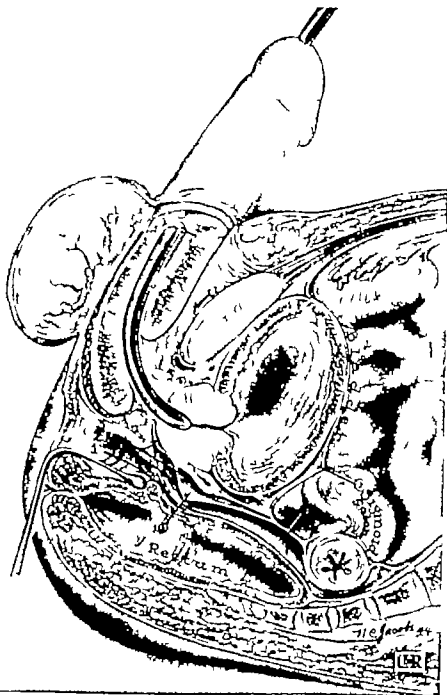


Fig. 30. Drawing sagittal pelvic section of a male cadaver in which the Young prostatic approach was made. The anus and lower part of the rectum are retracted dorsally within the incision. In this approach the rectal fascia was divided—part of it is still attached to the central point of the perineum; the remainder covers the cephalic portion of the rectum. The peritoneum is elevated from bladder and cephalic portion of the rectum. The anterior layer of Denonvilliers fascia is attached to the peritoneum and extends caudally between the seminal vesicles and prostate and rectal fascia, to the superior layer of the urogenital diaphragm. This membrane adheres to the prostatic capsule at the junction of the ejaculatory ducts to the prostate. Other fibrous bands extend from the peritoneum to the seminal vesicles and bladder. As indicated by the arrows, cleavage planes may be made between 1, the rectal musculature and rectal fascia (posterior layer of Denonvilliers fascia); 2, the rectal fascia and the anterior layer of Denonvilliers fascia; and 3, either this anterior fascial layer and the fibromuscular coverings of the seminal vesicles or it and the prostatic capsule. A sound is passed through the urethra but the prostate is not shown retracted dorsally by the sound. When the prostate is so retracted these fascial layers are compressed against the rectal musculature and dissection may lead into the rectum. $\frac{1}{2}$ normal size.

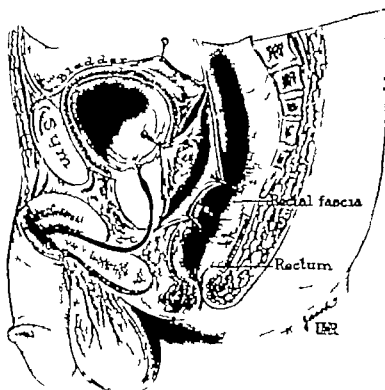


Fig. Oblique view of the sagittal section from male pelvis. The cephalic portion of the rectum is removed to show the rectal fascia covered by the lateral part of the anterior layer of Denonvilliers' fascia. This layer is retracted posteriorly and the seminal vesicles retracted anteriorly to show the posterior coverings of the seminal vesicles. The anterior layer of Denonvilliers' fascia and fibrous sheets from the seminal vesicles and bladder are attached to the pelvic peritoneum. $\frac{1}{2}$ normal size.

tween the prostate or seminal vesicles and the rectum.

The connective tissue around the rectal musculature and that around the epithelium of the seminal vesicles and prostate is derived from the mesenchyme surrounding these structures in the embryo. Since the seminal vesicles are an outgrowth of the mesonephric duct near the developing prostate and since this region is imbedded in a common layer of mesenchyme (Figs. 3, 5, 6 and 7) the fibromuscular connective tissue is continued around the prostate and seminal vesicles (Fig. 16).

Histological sections through the prostate of the young or old male contained a definite layer composed of smooth muscle and collagenous and elastic connective tissue which formed an outer covering and framework for the glandular cells of the prostate and seminal

vesicles. This tissue not only was continuous within the substance of the prostate and the seminal vesicles but also invested these glands. It has been stated that the covering of the prostate might be continuous with that of the bladder (Van Duzen, Looney and Duncan, 1939) and therefore the prostate could be considered as a gland at the neck of the urinary bladder.

As Wesson (1922) and others have suggested, the capsule of the prostate can be compared to the capsule of the liver or spleen—a surface layer of connective tissue surrounding an organ that is continuous with the connective tissue septa extending into the glandular portion of the organ. Our studies agree with this concept for where the glandular tissue was very near the surface of the fibromuscular covering a distinct capsule could not be dem-

onstrated histologically in many sections of prostates (Fig 16). In some sections of prostates showing benign hypertrophy the fibromuscular tissue on the surface and within the substance of the gland was increased (Fig 17). However in several sections of the prostate involved by cancer (Fig 18) the fibromuscular septa and the capsule were invaded displaced or replaced by adenocarcinomatous tissue. The latter condition could alter the glistening appearance of the fibromuscular layer of the prostate.

This fibromuscular tissue surrounding and permeating the glandular components of the prostate and seminal vesicles may be attached to or fused with the anterior layer of Denonvilliers fascia. The question then arises what is the anterior layer of Denonvilliers fascia and which tissues form the tough glistening layer the pearly gates over the posterior surface of the prostate? Is it the remains of the peritoneal cul-de sac together with the fibromuscular coverings of the seminal vesicles and prostate or merely the fibromuscular covering of these structures? Some descriptions of the perineal approach to the prostate intimate that the so called prostatic capsule and Denonvilliers fascia may be the same structure.

Our studies show that there are two layers of tissue covering the glandular elements on the posterior part of the prostate after the rectum and its fascia covering have been retracted. The membrane of fibrous tissue remaining from the cul-de sac of peritoneum covering the posterior surface of the prostate if well developed was thick and whitish in appearance. When this layer was incised and retracted the fibromuscular covering over the posterior surface of the prostate was exposed. The latter layer was also whitish and thick particularly in cases of benign prostatic hypertrophy. Therefore either the fibrous membrane or the fibromuscular covering of the prostate which usually were close together and were adherent at some points might form the glistening white layer known as the pearly gates. However histological preparations of tissue taken from the glistening white layer during perineal prostatectomy consisted only of fibromuscular and glandular

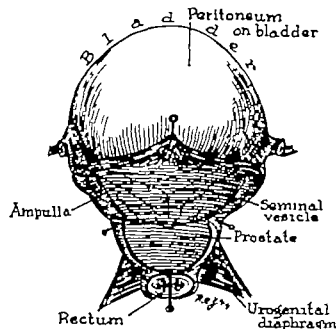


Fig. 22 Diagram of dorsal view of the anterior layer of Denonvilliers fascia. This anterior layer extends from the base of the prostate to the pelvic peritoneum between the rectum and bladder. It covers the posterior surfaces of the prostate and seminal vesicles and lateral extensions of this anterior layer cover the sides of the rectal fascia (posterior layer of Denonvilliers fascia). The upper part of the rectum and rectal fascia have been removed and the lower part of the rectum retracted posteriorly from the anterior layer of Denonvilliers fascia. The peritoneum covering the upper part of the rectal fascia is retracted forward. 3/5 normal size.

prostatic tissue. Therefore in many perineal prostatectomies the anterior layer of Denonvilliers fascia may be retracted backward with the posterior layer (rectal fascia) in the development of the incision (space 1 of Fig 20). The glistening layer in such instances would be no more than the fibromuscular covering of the prostate.

Our findings also agree with Denonvilliers description of the fusion of the prostatoperitoneal membrane with the connective tissue around the prostate forming a closed compartment around the base of the bladder (Fig 22).

Sections from various parts of the prostate and from the fibrous membrane posterior to the prostate indicated that part of the blood supply of the prostate courses in the fibromuscular covering and not in the fibrous membrane agreeing with Flocks (1943) description of the vascular supply of the prostate.

The importance of Denonvilliers fascia as an anatomic landmark in perineal surgery is well demonstrated by the frequent reference

to this structure in the literature. However a more detailed anatomic study of this fascia permits one to stress its relationship to other pelvic structures and especially to utilize the three potential spaces which can be developed during perineal surgery (Fig. 20). It becomes evident that if space 1 between the rectal fascia and rectal musculature (Fig. 20) is entered inadvertently one may damage the rectal wall or even enter the lumen of the rectum. On the other hand the rectal fascia constitutes a layer which can be used advantageously in the repair of rectal tears and recto-urethral fistulas (Scott 1935).

The fascia around the external rectal musculature may be areolar or both areolar and adipose depending on the body type of the individual. This layer has been described as the thicker posterior layer of Denonvilliers fascia and is the cleavage plane used in freeing and retracting the rectum backward in the perineal approach to the prostate. Although Denonvilliers did not describe this tissue as part of the prostatoperitoneal membrane but only stated (Fig. 2) "La face inférieure qui touche au rectum lui adhère à peine par un tissu cellulaire très-lâche" therefore by definition it should not be included in Denonvilliers fascia. However since this tissue is considered as part of Denonvilliers fascia in the clinical literature and for the sake of simplicity we suggest this fascia around the rectum be designated the posterior layer of Denonvilliers fascia. The fibrous membrane derived from the cul-de-sac of peritoneum could be designated therefore the anterior layer of Denonvilliers fascia. This terminology would help to clarify the descriptions of these fascial layers.

With the surgical development of spaces 2 or 3 (Fig. 20) the urological surgeon can have access to the prostate gland or seminal vesicles. It may be pointed out that if a sound or retractor is passed per urethram (Geraghty 1922 Johnson 1940 Lowaley 1940 and others) or if an instrument is passed per rectum (Foley 1920) the layers between the prostate and rectum were so compressed by pressure in our specimens as to render the separation of the natural cleavage planes in these layers more difficult (Fig. 20). In this respect the

procedure of Belt and coworkers (1939) offers some advantages since it does not use an instrument per urethram or per rectum in the first stage of the operation and therefore allows more space for dissection between the fascial layers.

Since cancer usually arises in the posterior lobe or may arise in any portion of the prostate (Moore 1935 Rich, 1935 Kahler 1939 and others) the fibromuscular covering over the prostate and seminal vesicles becomes an important barrier in limiting the spread of cancer. After direct extension through the prostatic capsule or into the region of the seminal vesicles and bladder the layers of Denonvilliers fascia would become the next line of defense (Figs. 20 and 22) in preventing the cancer from spreading posteriorly to the rectum. Furthermore spaces 2 and 3 shown in Figure 20 or both of these spaces may direct the flow of pus or urine extravasated from a ruptured prostatic abscess particularly the small pocket at the posteroinferior border of the prostate formed by the connection of the fibrous membrane (anterior layer of Denonvilliers fascia) to the posterior surface of the prostate at the level of the ejaculatory ducts.

The lithotomy position of the patient upon the surgical table may be varied greatly—from one in which the perineum is at an angle of approximately 45 degrees with the floor to the other extreme wherein the perineum is parallel with the floor. Belt and associates (1939) and Johnson (1940) use the latter position whereas Young (1926) and others use intermediate positions. It would appear from the standpoint of the anatomical location of the pelvic viscera and their fasciae that the Belt and Johnson procedures have the advantages of adjusting the pelvic structures to allow the surgeon to see the rectal fascia at all times and hence reduce the liability of rectal tears. Furthermore the extreme lithotomy position would bring the prostate closer to the surface of the perineum.

CONCLUSIONS

1. The tissue known clinically as Denonvilliers fascia was observed to be derived embryologically from two sources of connective tissue (mesenchyme) (1) a layer surrounding

the developing prostate and seminal vesicles and another layer around the rectum and (2) connective tissue (mesenchyme) adjacent to the mesothelium of the pelvic cul-de-sac of peritoneum. This peritoneal cul-de-sac extended to the level of the developing levatores ani muscles in young embryos.

2 The connective tissue around the seminal vesicles and prostate differentiates into the fibromuscular covering and framework continuous over both of these structures. That around the rectum differentiates mainly into the areolar or adipose tissue and musculature around the rectal mucosa.

3 With growth change in position and distention of the pelvic viscera the caudal part of the cavity in the pelvic cul-de-sac of peritoneum was obliterated progressively by approximation fusion and disappearance of the mesothelial surfaces. The connective tissue adjacent to the mesothelium remained as a fibrous membrane throughout development and was present in the adult.

4 The fibrous membrane derived from the pelvic cul-de-sac of peritoneum contained bundles of smooth muscle fibers. This membrane was V shaped and extended from the inferior border of the prostate to the pelvic peritoneum. The arms of the V extended laterally behind the seminal vesicles and on the sides of the areolar or adipose tissue around the rectal musculature. This membrane was near to the fibromuscular coverings of the seminal vesicles and prostate and fused with the prostatic covering at the junction of the ejaculatory ducts with the prostate. The endopelvic connective tissue (fascia) fused with the lateral sides of this fibrous membrane.

5 Fibrous bands also derived from the pelvic cul-de-sac of peritoneum which during development intervenes between the seminal vesicles and the bladder extended from the superior border of the seminal vesicles and posterosuperior surface of the bladder to the peritoneum.

6 We suggest that the fascia around the rectal musculature be designated the posterior layer and that the fibrous membrane which is derived from the pelvic cul-de-sac of peritoneum be designated the anterior layer of Denonvilliers fascia.

7 In the perineal approach to the prostate three potential fascial spaces could be developed between the rectum and prostate (1) between the rectal musculature and rectal fascia (posterior layer of Denonvilliers fascia) (2) between the rectal fascia and anterior layer of Denonvilliers fascia and (3) between the anterior layer of Denonvilliers fascia and the fibromuscular covering of the prostate and seminal vesicles.

8 Since the anterior layer of Denonvilliers fascia and the fibromuscular covering of the prostate were whitish in appearance and were close together or adherent either or both of these layers may constitute the glistening layer encountered in the perineal exposure of the prostate.

9 If the fibromuscular covering of the prostate were perforated by cancer or abscess the fibrous membrane (anterior layer of Denonvilliers fascia) may prevent direct spread of the malignant growth posteriorly to the rectum and may limit the spread of extravasated pus or urine.

10 The fascial spaces between the rectum, prostate and seminal vesicles were separated more readily in our specimens if they were not compressed by instrumentation per urethram or per rectum in the first stages of the perineal approach.

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THE FUNCTION OF THE PATELLA AND THE EFFECTS OF ITS EXCISION

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IT seems likely that more has been written about the patella, relative to its size than about any other bone in the human body and yet in spite of this there is no uniformity of view regarding its function. Lockhart described it as a lever and a roller bearing in the quadriceps tendon. Lickey, quoted by Brooke (5) attributed to the patella the function of a rocking lever whose fulcrum shifts distally as the knee joint moves from flexion to extension. Dubouix indicated a similar conception when he compared the patella to a gearbox which reduces movement and increases power. Walmsley Mackenzie and Jamieson all referred to it as a mechanical aid to the leverage of the quadriceps. Similarly Bowen Grant and Thomson expressed the conviction that the patella holds the extensor tendon forward away from the center of the knee joint, and so increases the leverage of its action. Thomson believed that this function is most important in the fully flexed positions of the knee. Heineck thought that the principal purpose is that of a pulley for facilitating the movements of the extensor tendon and that improvement in the leverage is a minor function. Jarecki claimed the same dual physiological rôle but he believed that these are secondary functions, assumed in the process of evolution and that the primary action of the bone as a block to prevent hyperextension of the knee has been lost. Bruce and Walmsley concluded from animal experiments that the patella's function is to protect the lower end of the femur against the traumatizing influence of the quadriceps tendon.

All the observers mentioned hitherto accredited the patella with a rôle of functional importance. The opposite view has however increased in popularity. From his case of con-

genital absence of both patellae with excellent knee function With concluded that the patella serves no useful purpose. Murphy (28) from observations on his cases of patellectomy considered that the bone is not essential for perfect mobility and function of the knee joint. De Vries decided that it is undergoing phylogenetic and ontogenetic retrogression and that it therefore plays no useful part in the body's economy. Powerful support was given to this view by Brooke (5) who claimed that his experimental and clinical investigations proved that the patella not only does not assist the action of the quadriceps on the knee joint but actually reduces its efficiency. Maróttoli made a similar claim.

In an attempt to establish the correct view of the patella's function the fields of comparative anatomy, human embryology, human anatomy, experimental anatomy and clinical surgery are examined.

COMPARATIVE ANATOMY AND HUMAN EMBRYOLOGY

The study in comparative anatomy and embryology has been reported elsewhere (19) and only the conclusions will be recapitulated here. There is no evidence that the patella is undergoing phylogenetic or ontogenetic retrogression and on the whole the evidence supports the view that it has a functional value in extension of the knee joint.

In the field of human anatomy the relationship of the patella to the extensor tendon of the knee has been disputed. The classical view as expressed by Poirier is that the quadriceps tendon is attached to the base of the patella, the patellar tendon is attached to the apex and these tendons are connected by a thin prepatellar aponeurosis and rather thicker medial and lateral retinacula. But Bernays and Kazzendar described the bone as lying posterior to the extensor tendon and only loosely attached to it. Brooke (5) and Hey

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This paper is based on an Arliss and Gale Lecture at the Royal College of Surgeons, London, on May 10, 1944.

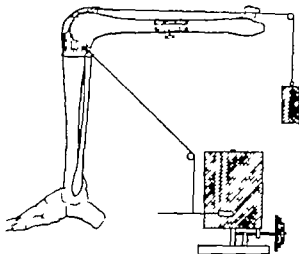


Fig. 1. Measurement of the range and speed of extension of the knee joint by a constant force

Groves (17, 18) subscribed to this view. It must be agreed, however, by all who have performed the operation that in the removal of the patella many fibers of the patellar and quadriceps tendons must be divided, and sagittal sections of the bone and its tendons show clearly that the patella gives attachment to the vast majority of the fibers of these tendons. Therefore the bone lies in the line of the extensor tendon and transmits the tension produced by the quadriceps. How else could it be rent asunder by sudden contractions of this powerful mass of muscle?

EXPERIMENTAL ANATOMY

The surest way of determining the function of the patella is to study the effect which its removal has on the knee joint. To this end experimental patellectomy has been carried out in animals and human cadavers. Bruce and Walsmsley, using rabbits, found degenerative changes in the patellar surface of the femur after patellectomy and they concluded that the patella protects the femur from trauma produced by the quadriceps tendon. It is an established fact, however, that when the articular surfaces of a synovial joint are separated degenerative changes take place in the hyaline cartilage. This may well be the explanation of the changes observed by these investigators.

Carey Zeit and McGrath used puppies and took special care to ensure that no perichon-

drium or periosteum remained in the tendon after operation. In spite of this regeneration occurred within a few weeks but did not do so if the knee was immobilized by arthrodesis.

After arthrodesis of one knee the weight was borne chiefly on the normal hind leg and the patella of that limb became larger than normal. These results suggest that the bone has a rôle of functional importance and they were supported by the findings of Girardi using dogs. On the contrary, Brooke (5) concluded that the patella is an encumbrance which reduces the efficiency of knee extension. The following investigation was carried out in order to determine which was the correct view.

METHODS

The knee joints of 7 cadaver limbs were mobilized by the division of all restraining structures and lubricated with a jelly so that they moved as freely as in life. Each limb was investigated in several ways at the following stages: (1) before patellectomy, (2) after removal of the patella either through a sagittal section of the bone and its tendons or after reflexion of the quadriceps distally by dissection of the entire bone from its bed leaving the thin prepatellar aponeurosis intact, (3) on replacement of the patella in its bed without attachment, (4) after suture of the quadriceps and patellar tendons together with obliteration of gap bridged by prepatellar aponeurosis.

Extension of the knee joint by a constant force. This investigation was similar to that of Brooke (5) with a modified apparatus (Fig. 1). The femur was clamped in a horizontal position and a pull was applied to the quadriceps tendon by a cord passing over a pulley to a hanging weight. The weight was such that under its influence the intact knee moved almost to full extension. Records of movement in each of the 4 stages mentioned were made on moving smoked paper (Fig. 2).

The law of moments states that for equilibrium the sum of the moments of a system of forces about any point must be zero. When the force of knee extension is balanced by a force acting at the ankle the conditions are as shown in Figure 3. A precise measure of the influence of the patella on the extensor apparatus of the knee should be obtained by a

TABLE I.—RANGE AND SPEED OF EXTENSION OF KNEE JOINT BY A CONSTANT FORCE—AVERAGE FOR 7 CADAVER LIMBS

	Angle reached—degrees	Time to reach angle A—seconds
Patella present	167	0.39
Patella absent	137(A)	0.35
Patella replaced	162	
Tendons sutured	150	

study of the forces *A* and *B* and the distances *x* and *y* before and after patellectomy.

Mechanical ratios. Spring balances were used to determine the forces one attached to the leg just distal to the malleoli and the other in turn to the quadriceps tendon and to the patellar tendon (Fig. 3). The position of the pulley *C* was arranged so that when the balance *D* registered 1 kilogram the center of gravity of the leg and foot was directly below the axis of the knee joint and the cord passed from the pulley to the leg in a horizontal direction. This ensured that the moment of force *B* remained constant and was the only factor resisting extension of the knee. The femur was tilted in the clamp so that knee joint angles of 60, 90, 120 and 150 degrees were obtained and at each of these the tensions necessary in the tendons to balance a resistance of 1 kilogram at ankle were found.

Distance ratios. The position of the axis of the knee joint was found by drawing the radii of curvature of the condyles on a lateral profile drawing of the lower end of the femur. These intersect in a small spiral indicating that the curve of the articular surfaces of the condyles is not a part of a circle but of a spiral, a fact which was noted a century ago by the brothers Weber. The center of the small spiral gives a fairly accurate axis for all positions of the joint and it coincides with the center of the femoral attachment of the lateral ligament. Measurements were made from this point to the central plane of the patellar tendon on profile drawings of the cadaver knee joints with a dioptrigraph (37) and also from same point to tip of lateral malleolus.

RESULTS AND DISCUSSION

Extension of the knee joint by a constant force. The results are presented in Table I. After patellectomy the leg stopped moving 30 degrees short of the angle reached when the



Fig. 2. Record of extension of the knee joint by a constant force.

patella was present. This is clear proof that the efficiency of the extensor mechanism in the more extended positions of the knee is seri-

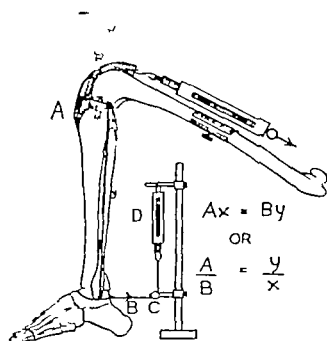


Fig. 3. The law of moments applied to the leg. Measurement of the ratios of the tensions in the quadriceps and patellar tendons to the resistance at the ankle.

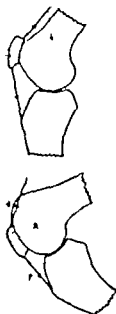


Fig. 4. The forces acting on the patella in the knee joint at 90 degrees and 100 degrees.

ously impaired by the operation. The original efficiency was almost completely restored by reinserting the patella in its bed. Suture of the quadriceps to the patellar tendon gave a 13 degree increase in extension. This indicates that in the more extended positions the retinacula do not transmit the pull of the quadriceps as efficiently as does the restored central tendon, contrary to the findings of Brooke (5).

Of the efficiency of extension between 90 and 135 degrees the best indication is the time taken before and after the removal of the patella for the leg to reach the angle at which it ceased to extend after patellectomy. This was determined from the graphs. Without exception the time taken after the operation was less than that when the bone was present. Excision of the patella resulted in increased efficiency of knee extension but only in the flexed positions and not as Brooke maintained throughout the whole range of knee movement. He reported that the leg moved at a constant speed after the initial acceleration and this was confirmed. This finding is of significance because the resistance to the movement of extension which is the moment of the leg's weight about the knee joint axis increases as extension proceeds. To maintain a uniform velocity the extending moment

TABLE II—RATIOS OF TENSIONS IN QUADRICEPS AND PATELLAR TENDONS TO RESISTANCE AT ANGLE AT DIFFERENT KNEE JOINT ANGLES—AVERAGE FOR 7 CADAVER LIMBS

Angle degrees	Patella present	Quadriceps tension			Patella tension	
		Patella intact	Patella replaced	Tendon sutured	Patella present	Patella absent
90	1	5	5			5
95		5			9.8	5
100	10				8	
105					7	10

must also increase despite the fact that the pull on the quadriceps tendon is constant. Since the leg stopped moving at an earlier stage after patellectomy, this increase in the extending moment with knee extension must be reduced by the operation.

Mechanical ratios. The average results are given in Table II. The decrease in the ratios which accompanies knee extension confirms that the extending moment of a constant tension in the tendons increases as the joint extends. Patellectomy produced a slight decrease in the ratio for the quadriceps tension at 60 and 90 degrees, confirming that the extensor efficiency in the flexed knee is increased by the operation. But the decrease in this ratio between 60 and 130 degrees was only 14.5 per cent against the 42.2 per cent decrease before patellectomy, indicating that the patella is responsible for most of the increase in extensor efficiency which accompanies knee extension and that its removal reduces considerably the efficiency of the movement of extension in the more extended positions.

The ratios for the patellar tendon tension were almost identical with the corresponding distance ratios (Table III); this finding confirms the application of the law of moments. At the same time they were less than those of the quadriceps tension and particularly was this so in the flexed positions of the knee and when the patella was present. This finding indicated that there is a loss of power in the transmission of tension in the extensor apparatus, and that the patella is largely responsible for the loss. To understand how such a freely gliding structure can cause a consider-

TABLE III—RATIOS OF AXIS-MALLEOLAR DISTANCE y TO AXIS-TENDON DISTANCE x AT DIFFERENT KNEE JOINT ANGLES—AVERAGE FOR 7 CADAVER LIMBS

Angle degrees	Axis-tendon distance		y to ratio	
	Patella present	Patella absent	Patella present	Patella absent
60	cm 3.8	cm 3.5	3	
90	4	3.5	0.6	
90	4.6	3.8	8.1	
90	5	4.0	7.6	0.0

able loss of power the various forces acting on it must be examined

The knee joint is considered in two positions 150 degrees and 60 degrees (Fig 4). The forces are the pull of the quadriceps Q the tension in the patellar tendon P and the reaction R from the femur acting through the point of contact of the two bones. These forces pass through one point when equilibrium is present and a triangle of forces is completed by drawing P' parallel to P . The sides of this triangle represent the forces in relative magnitude as well as in direction. At 150 degrees P is nearly equal to Q and at 60 degrees is much smaller which confirms the experimental findings. In addition the pressure between the patella and the femur indicated by R is greater at 60 degrees than at 150 degrees. This does not matter when the friction is negligible as it is normally but in states such as osteoarthritis, in which the cartilage is roughened and friction is greatly increased there is an increased loss of power especially in the flexed positions as was clearly shown in one of the cadaver legs. Marked patello-femoral osteoarthritis was present and considerable improvement in the efficiency of knee extension throughout almost the whole range of movement followed patellectomy and suture of the quadriceps and patellar tendons together.

Distance ratios The distance ratios indicate that the increase in the extending moment of a constant quadriceps tension which accompanies knee extension is due to increase in the axis-tendon distance the distance from the knee joint axis to the central plane of the patellar tendon. This increase is due mainly

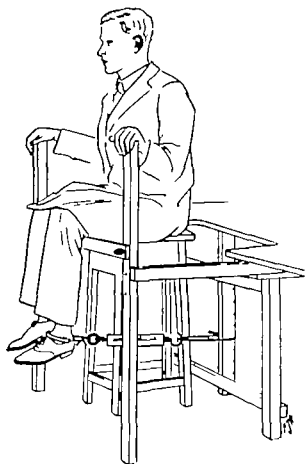


Fig. 5. Measurement of the power of knee extension

to the patella moving out of the intercondylar fossa where it lies in full flexion on to the anterior surface of the distal end of the femur

CLINICAL

The last field of study is that of the living. Good results following patellectomy have been claimed by many surgeons from Stimson on ward (2 11 12 27 29 34 37 40) the majority stating that after the operation the knee is functionally equal to normal. On the other hand Heineck Friberg and Wass and Davies concluded that the patellectomized knee has an impaired power of extension. Brooke (4) appears to have been the only one to measure quantitatively the effect of the operation. Using a dynamometer attached to the ankle he tested the power of knee extension with the knee joint at 90 degrees and found that this was slightly greater in the leg operated upon than in its normal counterpart.

The apparatus shown in Figure 5 was used in the present study. By raising or lowering

TABLE IV—POWER OF KNEE EXTENSION MEASURED AT ANKLE IN 7 NORMAL SUBJECTS AND 2 PATELLECTOMIZED

Angle-degrees	Normal subjects		Patient		Patient	
	Right leg	Left leg	Right leg	Left leg	Right leg	Left leg
60	3	30	3	3	5	24
90	24	3	30		8	5
120	43		44	33	8	3
150	44	4		3		27

Denotes limb in which the patella is absent

the cross bar supporting the thigh and also the attachment of the cord to the upright post behind the subject, and by adjusting the length of the cord between the post and the spring balance the maximum power of knee extension could be measured for each of the four chosen joint angles, with the leg vertical and the cord horizontal. These conditions are necessary to eliminate unrecorded variations in the moment of resistance to extension. Table IV gives the average results from 7 subjects.

The power of extension increases as the knee extends. This finding is of interest in view of the law of von Schwann that the tension of contraction diminishes as muscle fibers shorten. In the case of the quadriceps the fibers are shortest in the fully extended position of the knee joint, and therefore the tension which they can produce is least in that position. The fact that the power of knee extension increases in spite of this is further proof that the extending moment of the quadriceps pull increases as the knee extends.

It would be expected from the results of the experimental work that patellectomy would result in the loss of the greater part of the increase and this proved to be so in the two subjects examined. Both had a patellectomy performed several years previously and both had no functional disability in everyday life. Clinical examination revealed a thickening in the tendon where the patella had been. There was some quadriceps atrophy on the affected side especially in the second case but in spite of this the response to the usual clinical tests of function were normal. There was no limitation of flexion in either case and on the whole the end results could be regarded as

very satisfactory. But the dynamometer revealed the true state of the extensor efficiency (Table IV). At 60 degrees the power of extension was less than on the normal side. This confirms the quadriceps atrophy because with equal quadriceps the power of extension should be greater in the patellectomized leg at 60 degrees and 90 degrees. Loss of the patella resulted in a greatly reduced power of knee extension in the extended positions, and since these are the positions most important to man's activities it is correct to conclude that the operation makes the knee less efficient than the normal one. This loss of efficiency may not show clinically or be felt by the patient in everyday activities since the quadriceps possesses a large reserve of power but cases have been reported in which the functional efficiency is obviously below normal.

Applying the results of this study of patellar function to the surgical treatment of conditions involving the patella it can be said that since patellectomy definitely impairs the efficiency of the extensor apparatus of the knee joint the operation should be avoided when possible. It is indicated in conditions such as severely comminuted fractures and in inflammatory and neoplastic diseases of the bone. It appears to be indicated in osteoarthritis when this is mainly confined to the patello-femoral articulation for it has been shown in this study that the knee is likely to be more efficient after patellectomy and good results have been reported by Ludloff, Friberg, Berkheiser and Zeno and Maróttoli. Whether better results are obtained in simple transverse fractures by removal of the fragments or by the more conservative methods of fixation is still doubtful since no large comparable series have been reported. But it cannot now be claimed in favor of complete extirpation that function of the knee is thus improved.

With regard to the technique of patellectomy this work shows that for greatest efficiency the quadriceps tendon should be pulled down and sutured to the patellar tendon as advised by Maróttoli and by Friberg. The reason is that the central tendon restored by this suture transmits the pull of the quadriceps more efficiently than do the patellar retinacula. Furthermore the fibers of the quadri-

iceps muscle are stretched by this procedure and can therefore contract more strongly in obedience to the physiological law mentioned earlier. This stretching causes a reduction in the cross-section of the quadriceps which may be permanent. Though it might be thought permanently to limit flexion of the knee it does not in fact do so.¹

One other point of considerable practical importance is the great tension which the quadriceps can produce in its tendon and which the patella has to transmit. With the knee joint at 60 degrees a force of extension exceeding 40 kilograms at the ankle was achieved by several subjects. Since the average mechanical disadvantage for the quadriceps in this position is 15.4 : 1 the tension in the quadriceps tendon in these cases was more than 600 kilograms. No wonder that the patella is often snapped across the end of the femur by sudden contractions of the quadriceps and small wonder that it is the most frequently refractured bone in the body (8).¹ It is obvious that no sutures however skilfully inserted and however strong will withstand strains of a fraction of this magnitude and it follows that weight bearing movements of the knee after patellectomy or after suture of a fracture should not be commenced until the tissues have had time to heal strongly.

SUMMARY

1 The patella is a sesamoid bone developed in and lying in the line of the extensor tendon of the knee.

2 Its phylogenetic and ontogenetic development indicate it probably has a function.

3 Experimental work shows that the patella improves the efficiency of knee extension in the more important extended positions of the knee joint by holding the patellar tendon away from the axis and thereby increasing the extending moment of the quadriceps pull.

4 Clinical investigations confirm the experimental findings.

5 Patellectomy is justifiable in patello-femoral osteoarthritis.

6 In the operation of patellectomy the quadriceps tendon should be sutured to the

patellar tendon and quadriceps activity much restricted until healing is sound.

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¹Freely, personal communication.

ROENTGEN THERAPY AS AN ADJUNCT IN THE MANAGEMENT OF ACUTE POSTPARTUM MASTITIS

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ROENTGEN treatment of acute postpartum mastitis has been successful in Europe (Goetz, Cranio, Coedel, Hanne, Kautsky, Margraf, Pfalz, Pohl, Steinkamm, Thiers) and in the few clinics from which it has been reported in this country (Howard and Dodek, McIntosh 17-18). Widespread acceptance of this method of treatment has been hampered by (1) failure to realize that a co-ordinated plan of management of these patients is necessary even when roentgen therapy is given, (2) simultaneous combinations of conflicting forms of treatment and (3) delay in referring these patients for roentgen therapy until other methods of treatment have failed to relieve the patient.

In January, 1942, a co-operative plan of treatment of acute mastitis was undertaken by the departments of obstetrics and radiology. Since that time the only breast abscesses which have occurred have been in some of the patients initially treated by other methods at home and subsequently referred for roentgen treatment or in patients treated entirely by methods other than roentgen therapy.

The current report is based upon the methods used and results obtained in treating one hundred patients with roentgen therapy for acute mastitis between January 1942 and June 1944. Sixty of these patients developed mastitis while in the hospital on the obstetrical service and 40 patients developed the disease after leaving the hospital. During the same interval there were 15 patients with mastitis who were not referred for roentgen therapy, 9 of these patients having developed the disease in the hospital and 6 having been referred to the hospital for treatment. In the preceding 16 years of the hospital's existence 77 patients have been treated for acute postpartum mastitis, 31 patients having developed the disease in the hospital and 46 patients having been referred to the hospital for treatment.

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The recent increase in incidence of primary involvement, as well as increase in bilateral involvement from 24 per cent formerly to 37 per cent in the current series, has been the subject of much discussion, investigation and concern. Much of this increase seems to be related to a decrease in available trained nurses for care and instruction of patients, a shortage of resident and senior staff doctors, a marked increase in birth rate and difficulties in maintaining and replacing mechanical equipment related to obstetrical practice. Increased interest in the subject as a result of the method of treatment used can be discounted as a factor in the increase in the number of cases recognized in the hospital because the gravity of signs and symptoms in most of the patients were such that they could not be overlooked nor the diagnosis missed. At most there were 5 patients whose initial manifestations and subsequent courses were so mild that under former circumstances, they might have been classified as one day fever or one day fever-breasts. Most of the individuals who developed mastitis after leaving the hospital were referred back for roentgen treatment because of interest in or acknowledgment of the method. How many of these patients might have been hospitalized under earlier circumstances for other methods of treatment cannot be estimated. At any rate, only 6 of the 40 had to be admitted either from severity of toxic symptoms, home conditions, or suppurations.

DIAGNOSIS

The diagnosis of this disease is most accurately made by a combination of subjective symptoms and objective observations. Some patients note pain from cracked or fissured nipples from one to several nursing periods before the onset of mastitis. Then a portion of the breast becomes tender and fever aches, and chills occur. Other patients have an explosive onset of their symptoms with high fever, chills, aches, sweats, headache, coryza and what the patients consider or admit to be a little incidental tenderness of one breast. In the latter group urine cultures, uterine cultures, chest roentgenograms, and ear, nose and

throat examinations are sometimes in progress before it is realized that a breast infection could account for all the symptoms.

Objectively two types of initial infection of the breast are noted. They are differentiated into superficial or interstitial and deep or glandular mastitis. Neither form remains separately identifiable for many hours, so that most patients have a mixed type of involvement by 24 to 36 hours. The superficial type most often arises from infection introduced through cracks or fissures of the nipple and abrasions of the breast surface. When the lymphatics become involved erythema appears over the involved portion of the breast. As the infection spreads the deeper structures of the breast may become indurated. The glandular type of mastitis often results from infection in areas of stasis from incomplete emptying or obstructed milk flow. It is usually limited for several hours to one lobe of the breast where induration and tenderness are noted. Later as the infection spreads, a superficial erythema develops over the involved area. The ability of these deep or glandular infections to cause necrosis and abscess formation is well known; such complications sometimes occur within 48 hours from onset of symptoms. Unless recognized and effectively treated early the infection may spread from lobe to lobe until much of the breast becomes involved.

By requiring fever, local tenderness, and erythema as basic criteria for the diagnosis of acute mastitis, we have eliminated engorgement and caking as factors in this series. Other features of the disease which are useful as adjuncts in making the diagnosis are the time of onset, more common unilateral initial involvement, and leucocytosis.

Figure 1 illustrates the time of onset of mastitis in our roentgen treated and other groups. As in other reported series of cases the peak incidence occurred in the second postpartum week, sporadic cases occurred throughout the nursing period and a minor increase was noted at the time lactation was suppressed. We hesitate to make the diagnosis under the fifth postpartum day although we have seen 3 patients. We have been called to see several other febrile patients who had combinations of engorgement or caking and uterine infection, pyelitis, or respiratory infection. One patient with axillary lymph node tuberculosis was excluded on the second postpartum day because of bilateral matted tender lymph nodes, previous history and absence of definite symptoms in the breasts themselves.

Nine of the group not given roentgen therapy and 13 of the patients referred for roentgen therapy showed initial bilateral mastitis.

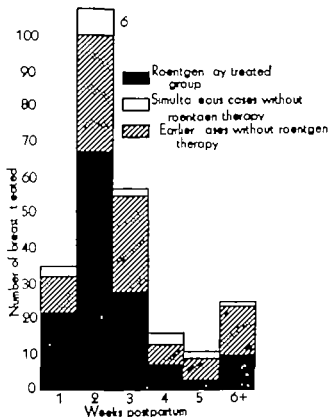


Fig. 1. Shows the time of onset of all the cases of acute postpartum mastitis diagnosed and treated in this hospital and its clinics.

The leucocyte count was above 10,000 in all but 2 of the roentgen treated and 3 of the other patients. The extremes in initial counts were 6,100 to 31,000. The average elevation of the roentgen treated group was 14,900 and in the other groups 14,400.

TREATMENT

The satisfactory management of these patients requires a co-operative plan among patient, nurse, obstetrician, and radiologist. The following subdivisions discuss most of the factors which make up a plan to insure comfort and speedy recovery for the patient and safety for the infant.

Roentgen therapy. The initial dose of roentgen therapy used in this series of patients varied from 40r to 100r and was dependent on the severity of manifestations of the disease and size of the area involved. The most acutely ill patients or those with large areas of involvement were given the small initial dose, while those with milder symptoms and smaller areas of involvement were given the larger initial dose of roentgen rays. The choice of kilovoltage filtration and target-skin distance was individualized for each patient. Patients with superficial infection only or those with small flat breasts with superficial or deep infections, were usually treated at 120 kilovolts.

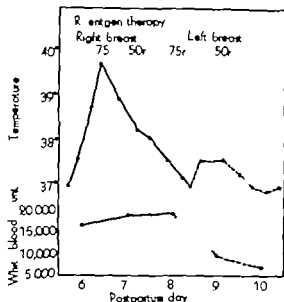


Fig. 4. Similar to Figure 3 but the leucocyt elevation is the function of the solid and broken line is apparently related to beginning mastitis in the opposite breast. Prompt treatment of the second breast when signs of mastitis became definite resulted in a comparatively mild course.

the second breast at the time the first breast was completely relieved by roentgen therapy. The second breast rapidly developed clinical signs of infection.

RESULTS

The results obtained from the use of roentgen rays as an adjunct in the treatment of mastitis in the series of 100 patients in this report are shown in Table I.

The results obtained from the use of other methods of treatment (mainly ice packs and occasionally heat or sulfonamides) on patients who developed mastitis during the same interval as the preceding group are shown in Table II.

TABLE II—RESULTS OF USE OF ICE PACKS, HEAT OR SULFONAMIDES IN OTHER PATIENTS DURING SAME INTERVAL

Onset in hospital				
Duration of symptoms before any treatment	Number breasts	Number cures	Number abscesses	Per cent abscesses
Less than 24 hours				
Onset after leaving hospital				
Duration of symptoms before any treatment	Number breasts	Number cures	Number abscesses	Per cent abscesses
Less than 24 hours	5		1	20
24 to 48 hours				
48 to 72 hours				100

TABLE III—RESULTS OF USE OF ICE PACKS, HEAT OR SULFONAMIDES IN MASTITIS PRIOR TO CURRENT SERIES

Onset in hospital				
Duration of symptoms before any treatment	Number breasts	Number cures	Number abscesses	Per cent abscesses
Less than 24 hours		8		8
Onset after leaving hospital				
Duration of symptoms before any treatment	Number breasts	Number cures	Number abscesses	Per cent abscesses
Less than 24 hours		3		3
24 to 48 hours	6		4	66
48 to 72 hours	4	3		75
More than 72 hours	6	9	7	44

Results which were obtained from the use of other methods of treatment (mainly ice packs and occasionally heat or sulfonamides) on patients who developed mastitis prior to the current study are shown in Table III.

Table IV gives a comparison of the preceding results with typical results from the literature.

EVALUATION OF METHOD

The literature on roentgen treatment of acute postpartum mastitis leads one to believe that striking relief from all symptoms occurs immediately after treatment. We have never noticed this in treating other infections such as furuncles, parotitis, and cellulitis and have not been surprised to find that the same type of interval exists between treatment and effect in this condition. It is granted that a few of our patients have been free from all symptoms two hours after treatment, but in any large series of patients there will be some mild infections which will subside quickly irrespective of treatment. Most of the roentgen treated patients actually do go through some type of crisis 4 to 8 hours after treatment, and thereafter do feel markedly improved. Careful tabulation of the maximum duration of all subjective symptoms and objective findings in the roentgen treated series reveals that the average duration of subjective symptoms is 1.88 days, and objective findings, 2.45 days. In contrast are the figures of the group not treated with roentgen rays in whom suppuration did not occur with an average of 8 days of subjective symptoms and 10.3 days of objective findings. The group operated upon had subjective symptoms from infection for an average of 44.6 days and objective findings for an average of 47.7 days per patient. No one knows definitely what reaction takes place in an irradiated infection of this type. We do know that the doses of roentgen rays used are

TABLE IV — COMPARISON OF RESULTS IN TABLES I, II AND III WITH THOSE IN LITERATURE

Author	Year reported	Treatment	Number patients	Number cures	Number breast abscesses	Percentage abscesses
Thoms	1915	Conservath	25	20	5	
		Early roentgen ray	20	2		8
Stekelman	1916	Conservath	47	35		5.5
		Early roentgen ray	34	3		6
Mangral	1916	Conservath	85	60	10	9
		Early roentgen ray	65	60	5	8
McIntosh	1910	Conservath	87	5	23	8.7
		Roentgen ray in 24 hours	36	35		7
		48 hours	14	6	8	57
St. Intosh	1911	Conservath	34			6
		Roentgen ray in 24 hours	75	74		5
		48 hours	50	18		55.5

infinitesimal as far as ability directly to affect the bacteria themselves (Duggar Wickhoff). Experimental evidence indicates that there is a transient hyperemia of microscopic proportion in the affected area (Dyes Tannenberg and Bayer) that leucocytes are attracted in increased number to the area (Osgood) that minor local chemical changes occur (Lieber Schoenholz and Hirsch Shade, Beck and Reimers) and that the whole process of defense against local infection is speeded (Desjardins).

The prompt recognition and admission of the possibility that there may be patients who will fail to respond to roentgen therapy is important in establishing opinions as to the value of the method. There is also the constant possibility that symptoms of infection elsewhere in the body can be superimposed upon some of those of mastitis and unless one acknowledges this he might treat a mastitis beyond actual necessity. One patient was changed from roentgen to sulfadiazine therapy because there had been no local improvement after 3 roentgen treatments in 36 hours and the other breast was developing mastitis. Nursing was stopped at this point. The infection subsided gradually but there were 2 recurrences of the disease during the next 6 weeks. The first recurrence responded to sulfadiazine and the last, a milder attack subsided with ice packs alone. The only unusual finding during the initial attack and recurrences was a white blood count ranging between 6 100 and 6 800 in spite of

fever above 104 degrees F for several days during the first attack 103 degrees F in the first recurrence and 101 degrees F in the second recurrence. Another patient was similarly changed from roentgen to sulfadiazine therapy because of only moderate improvement in the infected breast and a persistent white blood count elevation. Twelve hours after starting sulfadiazine a severe phlebitis of the legs became obvious, and 18 hours later mastitis developed in the opposite breast. The breast infection subsided without surgical intervention. Finally, a patient who showed good response locally to roentgen therapy continued to have a daily fever as high as 105 degrees F. The white blood count, which dropped to normal with treatment of mastitis, continued to drop afterward to 4 000. A chest roentgenogram and her subsequent course were consistent with atypical virus pneumonia.

Recurrences of mastitis in roentgen treated breasts have been unusual in reported series. One of our patients developed a second mastitis in another area of the breast 10 days after original treatment. One roentgen treatment brought about a cure.

Prophylactic irradiation of breasts with questionable or suspicious signs of mastitis has been recommended (Mueller) but we cannot endorse this procedure. There seems to be no more possibility of protection from such a procedure than from irradiating a foot because it is anticipated that a nail may be run into the foot. Since the action of roentgen-rays is mainly on the inflammatory reaction accompanying an infection no basis for prophylactic action would appear to exist.

All of the reports agree that there is no alteration in milk flow subsequent to the treatments. Although 3 of our patients noted decrease in milk flow after treatment, this is no more than can be accounted for on the basis of the infection itself. High fever temporary suppression due to ice packs or increasing pain. Information regarding nursing before and after the treatment discussed in this paper is available on 90 of the 100 patients: 7 never nursed, 14 ceased nursing before any signs of mastitis were present, 45 nursed before and after treatment, 24 were unable to nurse after treatment for the following reasons—(a) 3 refused to nurse after onset of pain, (b) 2 were admitted to the hospital and separated from the baby, (c) 3 had insufficient milk before and after treatment, (d) 3 had insufficient milk after treatment, (e) 2 had severe fissures of the nipples, (f) 11 had severe bilateral infection either simultaneously or in close sequence. Two patients

have gone through subsequent pregnancies and lactation periods without trouble, and a third patient developed bilateral mastitis with two successive pregnancies.

We have made no attempt to make a comparative evaluation of sulfonamides for this condition. Two roentgen resistant infections cleared when patients were placed on sulfadiazine, although one of these patients developed a severe mastitis in the second breast 18 hours after being started on the drug. Another patient had been on sulfadiazine for a week for an ear infection and developed bilateral mastitis while still taking the drug. In 2 other patients started on sulfadiazine 1 and 24 hours after appearance of the first symptoms of mastitis, abscesses necessitated operation 48 and 72 hours later respectively. We have avoided simultaneous treatment with sulfonamides and roentgen rays because of unsatisfactory results in other types of acute infections both experimental and clinical here (Sewell, Dowdy, and Vincent) and in the literature (Flocks, Fellows, and Kerr Kelly, and Dowell 11 12 Marks Tchaperoff). When these patients are seen early and there is no question of the extent of the disease, it seems more rational to treat the local area with roentgen rays than the whole body with chemicals in order to affect a local infection. Sulfonamides have the distinct advantage of availability for use everywhere, while roentgen therapy is limited to more densely populated areas.

We consider any breast infection which has existed for 48 hours or longer before being referred for roentgen therapy as a definite risk for abscess formation. If by local examination there is any suggestion of suppuration, we request the referring physician to perform a diagnostic aspiration of the area for pus. If pus is not found the chance is about 50 per cent of treating the patient without suppurative developing. If pus is found we give the referring doctor the choice of himself preparing the patient for surgery or having us give one or two preoperative treatments of 150 to 200 cc each in order to speed localization of pus, facilitate evacuation at operation and drainage subsequently.

A persistent objection to the roentgen treatment of these patients has been the cost. Referring doctors see a big difference between the cost of application of ice and roentgen therapy. The following summary of charges compares ward rates and private rates for various groups of patients with mastitis treated between January 1942 and June 1944. The charges are based on cost of hospitalization on either prolonged initial or readmission basis, operating room and anesthesia

fee and roentgen therapy. These charges do not include the professional fees of attending doctor or surgeons, but do include the radiologist's fee in all cases.

The average cost per infected breast treated during or prolonging patient's postpartum hospitalization period are as follows: Conservative methods—ward rate \$17.22 private rate \$27.50. Roentgen therapy method—ward rate \$9.12 private rate, \$19.35.

Average cost per infected breast treated after patient's initial discharge from the hospital but readmitted for treatment including surgical procedures when necessary. Conservative methods—ward rate \$54.00 private rate, \$84.50. Roentgen therapy method—ward rate \$26.55 private rate \$45.44.

Excluding the cost of those patients who had to be hospitalized in the preceding group the average cost of ambulatory treatment would be: Conservative methods—ward rate doctor's fee private rate doctor's fee. Roentgen therapy method—ward rate, \$4.60 private rate \$11.50.

SUMMARY AND CONCLUSIONS

1. Roentgen therapy combined with rational symptomatic treatment of 137 breasts affected by acute postpartum mastitis resulted in 2 abscesses, 1.5 per cent as compared with 20 per cent abscesses with other methods of treatment in use prior to this series. The 2 abscesses in the roentgen treated group occurred in patients initially treated by other methods and not referred for roentgen therapy until 4 and 7 days after onset of the disease.

2. The duration of subjective symptoms in these patients was reduced from an average of 8 days with methods of treatment other than roentgen therapy to an average of 1.8 days with roentgen therapy.

3. Application of roentgen therapy is so effective in the early stages of this disease that treatment should be started as soon as the diagnosis can be definitely made regardless of the hour. Delay in starting this treatment decreases chances of recovery without surgery.

4. A co-ordinated plan of management of these patients is necessary in order to secure the best results, and such a plan has been discussed in this paper.

5. Acknowledgement of infections apparently resistant to roentgen therapy is made and management of these patients is suggested.

6. Analysis of patient costs reveals that roentgen therapy is the cheapest form of therapy for acute postpartum mastitis.

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SUSPENSION OF THE UTERUS USING THE PFANNENSTIEL INCISION

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MALPOSITIONS of the uterus is a subject that has stimulated the imagination and ingenuity of gynecologists and surgeons for centuries. Some appreciation of this statement is forthcoming when we recall that more than 150 original operations and more than 300 mechanical devices have been designed for the correction of these conditions. All of this effort gives unmistakable evidence of the complexity and difficulty which these problems may present.

The multiplicity of procedures has added much to the confusion especially to the inexperienced. Though many of the operations have been discarded the subject is still not clear in the minds of a great many. A large group of these operations were designed in that period of gynecological history when it was the consensus that the uterus and other pelvic structures could be supported from above without respect to the integrity of the pelvic diaphragm. While this theory upon which many of these operations were based has been obsolete for more than a generation some of them are still popular wherever surgery is practiced not withstanding the shortcomings of these procedures.

It is not strange, therefore that these older operations, conceived and designed upon an untenable theory should be found upon close examination to be unsound in physiological anatomical, and surgical principle. Nor is it surprising that such operations should be subject to serious complications and malfunction of the uterus and other pelvic organs. To be more specific, these operations are represented by the Gilliam, the Ohlhausen the Doléris, the Kelly the Kocher the Leopold the Vineberg and their numerous modifications. Time and space, however do not permit a detailed discussion of these operations, but these generalizations at least serve to bring into focus the principles which we believe should underlie a suspension operation.

We are aware that gynecologists are reticent to attribute any function to the round ligaments. We believe that normally the round ligaments have the function of training the uterus forward

in anteversion and at the same time allow the uterus to rotate back and forth upon its transverse axis (at the level of Mackenrodt's ligaments) to accommodate the mobile demands made upon the uterus by its environment and its functions.

The revival of interest in the Pfannenstiel and other transverse incisions has, during the past years, resulted in a more extensive use of this incision by many surgeons. We believe, however that its usefulness is still unappreciated, more particularly by those who have not used it. This incision has several advantages and prominent among them, is its utility in a suspension operation to be described. As an incision, it represents a true gridiron and meets the important surgical requirements of a good incision in that it causes minimal injury to aponeurotic muscles, nerves, and lymph and blood vessels. It is for these reasons that it heals promptly leaves a strong abdominal wound resists infection and gives the best possible cosmetic result. We have gained the impression furthermore that it is attended with less shock and requires less postoperative analgesia than does the longitudinal incision.

On the contrary the incision has certain contraindications which should be borne in mind. It is not well adapted to large tumors above 6 or 8 inches in diameter. It is contraindicated in very obese women in whom the pelvic line is often buried very deeply below the surrounding skin. In these women this incision invites infection. Though it is seldom that pelvic surgery is performed in the presence of virulent infection, it probably should not be employed when such infections are known to exist, as the incision does not lend itself well to drainage. It has also been condemned on the ground of being time consuming but if this disadvantage exists, it is outweighed by the advantages which we have pointed out. We have not found it to be any more time consuming than the closure of the improved longitudinal incision that is, the opening of both rectus sheaths and subsequent approximation of the muscles and sheaths.

The details of the Pfannenstiel incision have been so well described by others that no further

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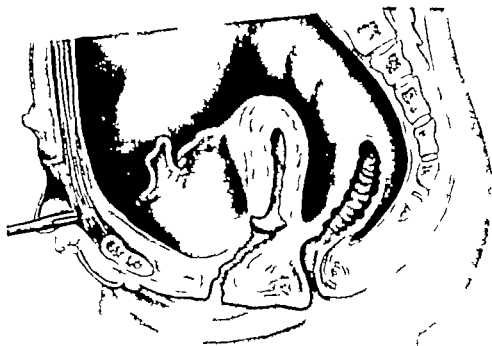


Fig. 1

Fig. 1 The instrument is introduced through the internal ring and then opened about 1 centimeter to grasp the round ligament about its midpoint.

description is required here. We do believe however that it is important to point out that the sight of election for this incision is through the pelvic line which is almost always present

THE OPERATION

Step 1 The usual Pfannenstiel incision is made and the peritoneum is opened. General inspection of the abdominal cavity is made and other necessary surgery is performed. The round ligament is then brought up into the abdominal wound by the following maneuvers. The first assistant retracts the right rectus upward and outward with his left hand. The operator makes gentle traction upon the right round ligament to the left to accentuate the exit of the ligament through the internal abdominal ring. With his left hand the operator inserts a long curved hemostat behind the aponeurosis into the internal abdominal ring which it should enter without appreciable resistance, lateral to the round ligament. The nose of the instrument should be visible through the peritoneum which the hemostat should perforate at or near the ring. The hemostat is now opened about 1 centimeter and the round ligament is grasped about its middle (Fig. 1) and then brought through the peritoneum and the ring and thence into the abdominal wound where it is caught with an Allis clamp and dropped into the angle of the

wound. The left round ligament is brought into the abdominal wound by the same technique except that functions of the first assistant and the operator are reversed. The result is carefully inspected to make sure that no knuckle of peritoneum is brought through with the danger of subsequent hernia formation.

Step 2 Both round ligament loops are now drawn mesially along the lower aponeurotic leaf until the uterus is brought into the desired position of correction. The position of the loops now determines the position at which the anchor sutures should be set and these points are marked by small notches in the lower aponeurotic leaf. The loops are dropped back into the angles of the wound. The anchor sutures cannot be set at this stage of the operation as they will interfere with the closure of the peritoneum and rectus muscles.

Step 3 After the peritoneum has been closed and the recti approximated the round ligaments are again brought to the point which is marked on the aponeurosis. The round ligaments are then sutured to the posterior surface of the aponeurosis with a mattress stitch of nonabsorbable material. The aponeurosis is then approximated and this continuous suture should go through but not around the ligament (Figs. 2-3). It is important not to remove the Allis clamp until the anchor sutures have been placed because, if this is

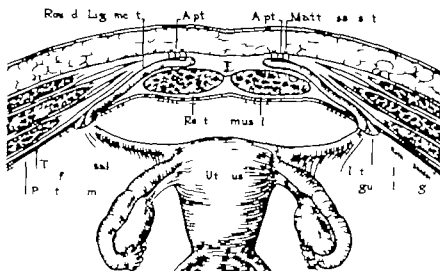


Fig. 3. The final relationship of the round ligament to the uterus and rectum. The uterus is the anchor point for the ligaments and is determined by the location of the ligaments. Each ligament is the best correction.

inadvertently done, the loops will slip back into the abdomen which will have to be reopened to secure them again.

SUMMARY AND CONCLUSIONS

The pattern of this operation is based upon our understanding of the normal which is in brief that the uterus is supported by Mackenrodt's ligaments, the pelvic diaphragm, and the round ligaments. It is a stable suspension operation which does not interfere with the normal free mobility

and functions of the uterus and other pelvic organs. The operation necessitates a minimum of trauma to the viscera and a minimal disturbance of normal anatomical lines and relations (Fig. 4). It eliminates the possibility of complications and handicaps that are known to follow most of the operations still in common use. The futility of suspension operations in descensus without adequate reconstruction of the defective supporting structures of the uterus, bladder and rectum must be emphasized again.

We have outlined a type of suspension which should produce excellent results, eliminate trauma to peritoneum, and do away with those intraperitoneal pockets which may produce obstruction.

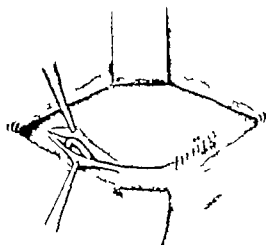


Fig. 4. The round ligaments are sutured to the posterior surface of the aponeurosis with a mattress suture and then caught in the continuous suture which closes the aponeurosis. (Some of these closures are done with interrupted sutures in the aponeurosis.)

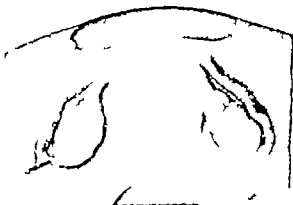


Fig. 5. Final position of the uterus. There is a minimum of intraperitoneal trauma and no pockets are formed.

We advocate the use of the Pfannenstiel incision for this procedure and for other gynecological procedures in properly chosen cases. The operation does not contraindicate pregnancy nor make delivery difficult as several of our patients who

have had suspension operations have gone on to normal delivery. By planting the round ligaments under the aponeurosis we bury the stumps which frequently prove painful and bothersome after their subcutaneous suture.

ADDING MORE SAFETY TO GASTROINTESTINAL SUTURES

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SURGEONS are in unanimous agreement that a good suture for the gastrointestinal tract should fulfill at least the following five requirements: (1) hemostasis—a requirement of paramount importance that cannot be overemphasized; (2) impermeability to liquids and gases under moderate pressure from within; (3) isolation—that is, after the repair is finished no part of the mucosa of the suture should be seen; (4) conservation of an adequate lumen for the unobstructed passage of the intestinal contents; and (5) unimpairment of healing—a requirement which is met by avoiding undue traction on the suture line and trauma to the tissues adjacent to the stoma.

Most of the intestinal sutures proposed by various authors for closing the anterior portion of the stoma have not been accepted with equal enthusiasm by surgeons, because of their failure to fulfill completely the five requirements stated. Of all the sutures which have been proposed that of Connell is the one most commonly used at the present time. However, this suture, as performed today and as illustrated and described in textbooks, does not seem to be completely hemostatic and hence does not fulfill adequately the first requirement given. It leaves free islands of intestinal wall between the loops of the suture, a serious drawback especially for the abundantly vascularized gastric and jejunal mucosae. This fact is illustrated in the accompanying Figures 1 and 3.

Moreover, these free islands created by the Connell suture might also be weak points at which leakage could occur when the intraluminal pressure becomes increased. This statement can be appreciated if we take into consideration that the union of a sutured bowel begins by a deposit of coagulated exudate which results from the trauma

inflicted by the needle and by the presence of the suture. Consequently if the sutures are spaced far apart—and this happens in the Connell suture unless the operator is particularly meticulous—or if the edges are not well approximated, adequate closure of the gastrointestinal wound is not obtained.

To correct the deficiency of the Connell suture and especially to achieve better hemostasis, the following suture for the anterior part of the stoma is proposed as illustrated in Figures 2, 4, and 5.

TECHNIQUE

Only the technique for the closure of the anterior portion of the stoma will be described in detail; the other steps are mentioned simply to consider the anastomosis adequately.

After the two segments of the alimentary tract, which are about to be anastomosed, are placed in proper apposition by rubber covered clamps, they are united by a continued seroserosal suture of cotton thread. This suture must be placed toward the mesenteric border of the intestine near the clamps in order to allow enough space for the posterior through and through suture after the two apposed visceral organs are opened.

The posterior continuous seroserosal suture starts a little beyond one extremity of the stoma and ends a little past the other extremity where it is advisable to knot it and so prevent puckering of the anastomosis. Both ends of the suture should be left long with the needle still threaded and laid aside, covered with gauze, to be used later. The opening of the apposed viscera usually is started with a scalpel about $\frac{1}{4}$ centimeter from the continuous seroserosal suture and finished with a pair of scissors. The length of the opening varies according to the contemplated function of the stoma. The cavities of the organs are aspirated and cleaned. If the mucosa is very redundant, part of it is excised and trimmed. With the cavi-

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Fig. 3. Showing Connell suture showing the free ends of mucosa, intestinal or of hernial sac, no leakage, compare this figure with figure 4 and note the free strand almost in the hernial sac, the suture is

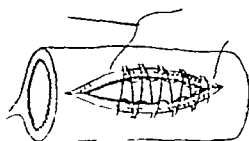


Fig. 4. Showing Connell suture showing the free ends of mucosa, intestinal or of hernial sac, no leakage, compare this figure with figure 3 and note the free strand almost in the hernial sac, the suture is

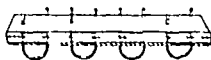


Fig. 5. Schematic presentation of intestinal mucosa and loops of Connell suture showing the free ends of the suture thread, no leakage, compare this figure with figure 4

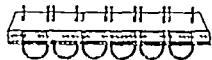


Fig. 6. Showing intestinal mucosa, the loop of the suture thread, the free ends of the suture thread, no leakage, compare this figure with figure 5

ties of both organs opened union of the first and second portions of the stoma is effected with a through and through intestinal suture. Beginning at one extremity the needle is passed from the mucous surface of one viscus through its wall to its serous surface and then from the serous surface of the opposite

viscus into the cavity of the latter. The needle comes again to the mucosa of the first organ about one centimeter in front of the previous suture and the same maneuver is repeated until the other extremity is reached. If desired the suture may be knitted from time to time to prevent pulling.

As the surgeon reaches the angles of the stoma he should continue carefully beginning the approximation of the anterior margins of the approximated viscera. To bring the angles of the stoma together the needle is passed from the mucous surface of one viscus to its serous surface then from the serous surface of the other viscus to its mucous surface after which the suture is drawn tight and the process is repeated by starting again from the mucosa of the opposite viscus until the angles of the stoma are successively inverted.

When the angles of the stoma are inverted the closure of the anterior portion is begun by the use of the proposed modified suture. The same needle that was just used to complete the inversion of the angles of the stoma threaded with the same thread after it is made to enter one organ from its serous surface toward its mucous surface is advanced about $\frac{1}{2}$ or $\frac{2}{3}$ centimeter according to the thickness of the organ. Thereby perforating the mucosa and serosa of the same side loop of the suture is formed on the mucosal side. Then the needle is inserted into the serosal side of the opposite organ perforating the wall and entering its cavity within a millimeter of the previous suture at this side. The needle is advanced again at

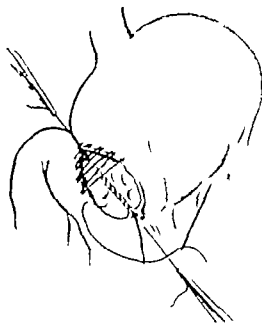


Fig. 7. Showing gastroenterostomy with modified suture being joined

the mucosal side $\frac{1}{8}$ or $\frac{1}{4}$ centimeter as stated before it pierces the mucosa and serosa from within outward. Then the cavity again is entered by the needle from the opposite side at a distance of about 1 millimeter from the previous suture. The process is repeated exactly in the same way until the entire intestinal wound is closed.

When the entire circumference of the stoma has been united by this modified through and through suture, the catgut thread is tied to its original end at the starting point and cut short. The seroserosal suture previously laid aside is now resumed reinforcing the anastomosis on its anterior aspect and completing the circumference of the wound to its starting point where it is to be tied to its own initial end and cut short. Few interrupted seroserosal sutures placed at the stomal angles and other points, complete the anastomosis without overcrowding the stoma with foreign material or jeopardizing its potency with undue infolding.

The accompanying illustrations, Figures 2, 4, and 5 will help to clarify the description as just given and portray the hemostatic effect of such a suture in comparison to that of the commonly

used Connell suture, as illustrated in Figures 1 and 3.

SUMMARY

It is assumed that the basic requirements that make a suture of the gastrointestinal tract safe are (1) complete hemostasis (2) impermeability (3) isolation (4) creation of an adequate lumen for the passage of its contents (5) noninterference with healing. The Connell suture, the most commonly used by the majority of surgeons for the closure of the anterior surface of the stoma, does not fulfill all of these requirements, because it leaves free islands in the approximated edges which render the suture not completely hemostatic and leakage proof.

For the correction of this deficiency a modification of the Connell suture is proposed and described.

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ACUTE PEPTIC ULCERS FOLLOWING DISTANT OPERATIONS

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AMONG the various complications of peptic ulcers, perforations and hemorrhage are two which require prompt and often heroic attention. It is generally agreed that in 15 per cent of all cases these complications occur as the initial and only manifestation of the disease (2). Fortunately acute peptic ulcers with or without hemorrhage or perforation following operations on other than the upper intestinal tract, are rare and for this reason perhaps, offer bewilderment to the unsuspecting surgeon. A thorough search of the medical literature of the last 20 years reveals literally hundreds of articles on various aspects of peptic ulcer but only very few that are concerned with an acute onset developing in an otherwise uneventful postoperative convalescence.

In 1925 Silver reported a case of thyrotoxicosis that developed signs and symptoms of gastrointestinal hemorrhage on the 6th postoperative day and died shortly thereafter. A postmortem examination disclosed an acute perforating ulcer of the first portion of the duodenum which had eroded the superior pancreaticoduodenal artery and so produced the fatal hemorrhage. In 1932 Cushing reported 3 cases in which patients died of acute perforation of the upper gastrointestinal tract after what were apparently successful operations on the cerebellum and on 9 others in which patients showed gastric erosion gastric malacia and chronic ulcer both as a result of operation on the brain and otherwise increased intracranial pressure. Because his interest was focused on the diencephalon as a possible para sympathetic center whose disturbance was responsible for the acute ulcers, he carefully reviewed the pertinent literature of the previous hundred years dealing with the neurogenic causes of peptic ulcer and cited a number of reports of similar cases. In 1935 Grant described 2 cases of acute duodenal ulcer following intracranial operations, one of which perforated. The following year Vale and Cameron described the case of a 55 year old man treated for fractures after an automobile accident who on the 21st day following admission developed severe abdominal pain

nausea and vomiting as a result of a perforated acute ulcer of the first portion of the duodenum. Finally, in 1940 Penner and Bernhelm collected from the literature at least 19 cases of gastrointestinal bleeding and acute ulceration of the stomach and duodenum. To these they added 47 cases of their own that showed both erosions and ulcers of the esophagus, stomach and duodenum. All of these cases, however were not postoperative for they also included diabetic acidosis and other conditions.

In a consecutive series of 1750 necropsies performed at the Jefferson Medical College Hospital in the last 5 years, there were encountered 5 instances of acute peptic ulcer that occurred following operations on other than the upper gastrointestinal tract. They are reported (1) because it is generally not realized that such ulcers may develop following distant operations on other than the brain and (2) because they again emphasize the importance of routine postmortem examination without which none of these cases would have been diagnosed.

REPORT OF CASES

CASE 1. A hit man 65 years old admitted to the hospital with a history of intermittent colic like pains in the right lower quadrant of the abdomen for months and vomiting for month. There are no previous gastrointestinal symptoms. Physical and ray examinations disclosed carcinoma of the ascending colon. Because the patient's physical condition was too poor for an extensive resection, a colostomy as first performed followed in several weeks by resection of the entire lower colon. The latter as performed under spinal anesthesia in 3 hours. The patient tolerated the operation very well and as in good condition upon his return to the ward.

The immediate postoperative convalescence as uneventful. On the 9th day after operation the Wangenstein and nasal tubes were removed and low residue diet was started. Four days later he said he did not feel so good and in the next 24 hours had several successive black stools in bed, ceased bright red blood three times. His total estimated amount of 2,200 cubic centimeters, became cold, clammy pale, confined and listless, showed drop in erythrocytes from previous normal 4,200,000 per cubic millimeter and in hemoglobin to 49 per cent and progressive decline in blood pressure. 1 unit of transfusions of blood and plasma he died about 36 hours after the onset of his first symptoms.

Necropsy as performed 3 1/2 hours after death. There was no peritonitis. The stomach was greatly dilated and filled with dark red fluid and clotted blood, and "coffee

From the Clinical Laboratories, Jefferson Medical College Hospital.



Fig. 1 Case 1. An acute ulcer of the central portion of the lesser curvature of the stomach. The stump of the eroded vessel cannot be seen in the photograph.

ground" material. The mucosa of the central portion of the lesser curvature disclosed a sharp recent ulcer measuring 1.5 by 3 centimeters across and 0.2 centimeters deep (Fig. 1). It was irregular in outline possessing a number of short projections into its lumen and disclosed slight undermining of its edges. Its floor was clean and was formed by the inner surface of the muscle coats. From its central portion there protruded into the crater the stump of an eroded vessel which measured 0.2 centimeter in diameter. Its end was covered with a dark red thrombus. The base of the ulcer was firm and red to gray. Its edges were dark red. In the immediate vicinity the mucosa disclosed 8 satellite erosions and ulcers measuring as much as 0.5 centimeter in diameter and penetrating the mucosa to various levels. Some extended to the submucosa. The mucosa of the body and fundus contained 9 or 10 other similar superficial erosions. The entire ileocecal region was absent and the right side ileocolostomy was healing well. The suture lines were intact and the ostium was patent. There were several superficial mucosal erosions in the terminal ileum. The mucosa throughout the rest of the small intestine and that of the large intestine was intact. The lumen of both the small and large bowel was filled with black fecal material. There were only a few leukocytes around the operative site and as far as could be determined there was no evidence of trauma to any of the structures in the upper abdomen.

The superior mesenteric vein at its entrance into the portal cist contained a recent antenormal thrombus measuring 3 centimeters in length. Nowhere was there any gross evidence of residual or metastatic carcinoma. The lungs were pale pink each weighing about 325 grams. They disclosed no congestion nor did they show any pneumonia. I emulsion to examine the brain was not granted. There were no other contributory findings. The surgically removed ileocecal portion of the intestine showed large kerating and stenosing carcinoma of the ascending colon with no gross displacement of the draining lymph nodes.

Microscopic sections of the tumor mass in the ascending colon disclosed nodular adenocarcinoma. There was no metastasis to the surrounding lymph nodes. Many sections were taken of the large ulcer of the stomach together with adjacent ulcer of the renal, smaller ulcers and erosions. In addition to numerous sections were also made of the entire thickness of the stomach wall centimeter away from the erosions and ulcers particularly where vessels were seen to enter the defect. All sections of the ulcers and erosions



Fig. 2 Case 1. An erosion of an artery in the base of the ulcer shown in Figure 1. Elastic tissue stain $\times 35$.

showed essentially the same process and differed only in the extent to which the wall was penetrated. Very early only the most superficial portion of the mucosa was defective assuming a small saucer shaped depression. In these there was no surrounding zone of necrosis or inflammation. Where the defects had penetrated to the submucosal mucosa they were still saucer shaped although the edges were somewhat steeper. Both they and the floor were covered with a layer of fibrin and ulcer fragments intermingled with which were polymorphonuclear leukocytes, plasma cells, and lymphocytes. The submucosa and underlying vessels were entirely normal. The third stage was a penetration of all the coat to the muscle layers. In these the edges of the mucosa were undermined and the entire defect was covered with an inner zone of necrosis, and intermediate zone of polymorphonuclear leukocytes, and nuclei fragments and an outer zone of granulation tissue composed of loose edematous fibroblasts, capillaries and varying numbers of polymorphonuclear leukocytes, plasma cells, and lymphocytes. The inflammatory cells penetrated along the connective tissue between the muscle bundles and including the serosa. The process was exactly the same in the largest ulcer except that there was more undermining of the mucosa that about one half of the inner surface of the muscle coat necrosed and that there was more inflammation of the surrounding tissue. The center of this ulcer there was a fairly large artery which showed a complete destruction of that portion of its wall in contact with the ulcer and thus a communication of its lumen with that of the stomach (Fig. 2). An adjacent vein showed a complete penetration of that portion of the wall facing the ulcer by inflammatory cells and granulation tissue without, however, causing a rupture. The outer portion of both the artery and the vein showed no pathological changes. Of the many vessel examined in section centimeter away from the erosion and ulcers only 3 showed a slight increase of the subintimal connective tissue reducing the lumen to about two thirds of its normal caliber. 2 vessels and 1 one half its normal caliber in one other. Thromboses or inflammation were not seen in any of the arteries.



Fig. 3. Case 3. Ulceration of the ileum. The inner surface covered the necrotic material followed (turn) by ones of polymorphonuclear leucocytes, fibrin and gran inflammatory cells. The serosa covered the acute exudate. (Hematoxylin and eosin, $\times 150$.)

CASE 3. A girl, 3 years old, admitted the history of exenteration in four years that was associated with colic prior for 5 years. In the last 3 months, he developed fatigue, weakness, and had recurrent pain in the right lower breast. Her appetite was not very good but she tolerated food. She and her head also had pain in other joints and had gait on the area of physical exertion. She had bronchoscopic examination in diagnosis of bronchiectasis of the right lung. She made 34 days after admission, right pneumonectomy performed under general anesthesia. Her use of very dense fibrinous pleural adhesions, the operation quite difficult and the patient emerged in danger of the procedure. She died 7 days later.

The following day, although her temperature and pulse were slightly elevated, as ordered that he did. On the 3 day after operation, however, she began to vomit, crying, and she showed no day later she complained of nausea and vomiting. Her general condition was not sound. Her last day of the pericardial cavity, which on culture showed streptococcus hemolyticus and nonhemolyticus. On the 6th postoperative day, the pericardial cavity was drained after which the patient became comatose and then totally irrational. She died 7 days following the pneumonectomy. The erythrocyte count was 4,000,000 per cubic millimeter before the operation, 4,800,000 on the second day after operation, and 3,500,000 just before death. The blood pressure was normal throughout except just prior to the operation of the pericardial cavity.

Necropsy was performed 12 hours after death. The peritoneal cavity contained 500 cubic centimeters of bile stained fluid composed of mucus, blood clots, and fibrin. The latter was particularly abundant along the inferior



Fig. 4. Case 3. An acute ulcer of the duodenum penetrating into the pancreas.

surface of the liver and around the gall bladder. The first portion of the duodenum just distal to the pylorus contained a mirror defect of the entire anterior and posterior wall each 2 centimeters long and 1 centimeters wide. The edges of the perforated wall were cut sharply, covered with an exudate, not indurated, and composed of all the layers of the wall in their normal anatomical arrangement. The mucosa of the stomach and of the remainder of the small intestine and the large intestine was normal. The serosal surfaces of the gut were adherent to each other by mucoid material.

The right lung was hyaline. The corresponding pleural cavity was reduced in size and the surfaces were covered with thick fibrinopurulent exudate. The left lung was emphysematous and showed no bronchiectasis. The pericardial cavity was obliterated by thick fibrinopurulent exudate. The heart was otherwise normal. The mediastinal structures appeared undisturbed. Permission to examine the head was not granted. The surgically removed lung showed extensive bronchiectasis.

At microscopic sections of the edges of the duodenal lesion disclosed complete penetration of the entire wall (Fig. 3). The edges were sharply angled and were covered by an inner zone of necrotic material followed by a layer of polymorphonuclear leucocytes and plasma cells. I adhered to this there sharply defined zone of fibrin in which there were only few inflammatory cells and nuclear fragments. Beyond this area the tissue was somewhat edematous and contained scattered polymorphonuclear leucocytes and plasma cells. The serosa covered the thin layer of exudate consisting of fibrin and round cells of inflammatory origin. The vessels in the duodenal wall were normal. Only the very superficial portion of the pancreas was necrotic. The lungs showed congestion, edema, and terminal pneumonia. The pericardium was covered with an exudate of fibrin, polymorphonuclear leucocytes, and round cells. There were no other noteworthy findings.

CASE 3. A boy, 7 years old, admitted the history of pain in the upper breast and numbness and tingling of both legs of 4 weeks duration, gradually increasing each new developed in the legs until 1 week before admission when they became completely paralyzed. There was no tingling of the hands, no local twitching. His appetite was fair and there was no history of belching, epigastric distress, or tarry or clay colored stools. Physical examination disclosed spastic paralysis of both legs, flaccid bowels, few

hot water bottle burns of the skin over the lower abdomen, and superficial ulcers over the bony prominences of the legs and pelvis. A diagnosis of spinal cord tumor was made a day later a laminectomy from the second to the fifth dorsal vertebra was performed under gas and ether anesthesia. Although the immediate postoperative course of the patient was good his condition rapidly deteriorated and he died 14 days after the operation. Just before death his temperature was 96 degrees F., pulse 120 per minute, and respirations 28 per minute. During his stay in the hospital 4 erythrocyte counts varied from 3,400,000 to 4,000,000 the hemoglobin from 61 per cent to 70 per cent, and the blood pressure from 80 to 100 millimeters of mercury systolic and 40 to 65 millimeters diastolic.

Necropsy was performed 2 1/4 hours after death. The body was emaciated and there were superficial ulcers of the skin of the abdomen, sacrum, gluteal regions, thighs, and heels. The posterior wall of the duodenum 2 centimeters from the pylorus contained a punched out recent oval ulcer that measured 0.5 by 0.7 centimeter across and 0.5 centimeter deep (Fig. 4). The edges were finely irregular and undermined for distances of 0. to 0.5 centimeter. The base was granular hemorrhagic, and showed no fibrosis. Most of it appeared to be composed of the muscle coats but along the left border there was a complete perforation of the entire wall into the underlying pancreas that measured by 0.6 centimeter. The pancreatic tissue was superficially brown and necrotic. The superior pancreaticoduodenal artery was found within the substance of the pancreas 0.5 centimeter beneath the base of the ulcer. Its external diameter was 0.3 centimeter and its lumen 0.05 centimeter across. The latter contained a red thrombus for a distance of 2.5 centimeters but showed no other gross abnormalities. The rest of the gastrointestinal tract was entirely normal.

There was no infection of the operative site. Below the level of the surgical incision from the fourth dorsal to the eighth dorsal vertebra there was a soft mushy gray fungating tumor mass filling the spinal canal and involving the surrounding bone. The brain showed marked congestion of the pia arachnoid vessels but on coronal sections which included the brain stem did not disclose other abnormalities. The remaining organs showed no contributory pathological changes.

Microscopically there was a sudden and complete interruption of the mucosa of the duodenum with penetration of all the coats to the surface of the pancreas (Fig. 5). The mucosal edge of the ulcer was covered with a slight amount of necrotic material, lymphocytes, plasma cells, and polymorphonuclear leukocytes. The latter extended into the mucosa for varying distances. The surface of the undermined mucosa together with the edges of the submucosa, muscle coats, and serosa were covered with an external layer of necrotic material and fibrin in which there were only scattered polymorphonuclear leukocytes and nuclear fragments. Beyond this there was a zone composed almost entirely of polymorphonuclear leukocytes next to which there was a broad band of granulation tissue. The latter was composed of a background of loose edematous connective tissue which contained thin and thick walled capillaries and varying numbers of polymorphonuclear leukocytes, lymphocytes, and plasma cells. This granulation tissue covered but only superficially penetrated the pancreas. Sections through the grossly visible area of perforation disclosed an intact pancreatic surface overlaid with only a thin layer of similar granulation tissue. The superior pancreaticoduodenal artery showed no histopathological change. It was filled with well preserved erythrocytes but showed no ante mortem thrombus.

CASE 4. A white man 57 years old was admitted with a history of cough with expectoration of 6 ounces of sputum



Fig. 5. Case 3. An undermined and collapsed mucosa. The floor and base of the ulcer are covered on the inner surface with necrotic material and fibrin followed by a zone of polymorphonuclear leukocytes and beyond this by granulation tissue. Hematoxylin and eosin, $\times 35$.

daily for one year and asthma for 9 months. He had no gastrointestinal symptoms but did lose 40 pounds in weight in 5 months. Physical, roentgen-ray and bronchoscopic examinations disclosed an abscess of the lower lobe of the left lung. Following several bronchoscopic drainages his temperature gradually came to normal. Two months after admission the abscess was drained externally through the chest wall under local anesthesia. During the operation a large vein was severed from which he bled freely. Hemorrhage was controlled by pressure and the cavity was packed with sponges. Following a blood transfusion he was returned to the ward in good condition. Three days later the packing was gradually removed and gauze was inserted into the cavity. In more days this was replaced with drains but 3 hours later the cavity was again packed because of bleeding. The next day when the packs were removed there was a sudden gush of blood from the cavity accompanied by hemoptysis, cyanosis, collapse and death.

Necropsy was performed 3 hours after death. The cavity in the lower portion of the left lung was filled with a blood soaked gauze and its surface was ragged. The remainder of the left pleural cavity was obliterated with dense fibrous adhesions. The bronchi of the entire left lung and those of the upper lobe of the right lung showed marked cystic dilatations that were filled with a black fluid possessing a foul odor. The stomach was dilated and contained food remnants stained with blood. The gastric mucosa disclosed scattered petechial hemorrhages along the lesser curvature. Directly upon the pyloric sphincter there was a small ulcer possessing sharp margins and hyperemic sloping walls. It measured 0.4 centimeter in diameter. Immediately beyond the pyloric sphincter the duodenum disclosed a "chronic healed" ulcer measuring 0.5 centimeter in diameter and showing a smooth gray base. The rest of

duration in days or at the most a few weeks rather than months or years. There were furthermore no scars to indicate previous ulceration. All her symptoms on the other hand are compatible with those resulting from an ovarian carcinoma.

In considering the cause or causes of the ulcers in these cases one is at once confronted with the cause or causes of any acute peptic ulcer and these have been adequately discussed in the literature from time immemorial. Since the many theories have been recently summarized by Cushing, Harkins, Venderahe, Moon and others they will not be reiterated here. A very few pertinent comments however do appear to be in order.

Because these patients were all operated upon shock as a causative agent must first be considered for in the opinion of Moon and Penner and Bernheim this phenomenon decidedly plays a rôle in the formation of some peptic ulcers. Unfortunately an unequivocal statement as to its presence or absence in these cases cannot be made for the history records are sadly lacking in the single best criterion for shock, namely hemocoagulation. Judging from the operative and postoperative record however it is quite unlikely that it played any part in the formation of the ulcers in Case 1 for this patient withstood operation excellently and his convalescence until the hemorrhage supervened was entirely normal. Operative shock may have played a rôle in Case 2 for the condition of this patient was not good during the operation and in Case 3 the patient was obviously a 'poor surgical risk' even before the operation. Although the operations in Cases 4 and 5 were performed under local anesthesia this procedure plus the subsequent hemorrhages might have been a contributing factor in the etiology.

Very little can be said about neurogenic factors for in only 1 case was the brain examined. In none of the cases however was there any gross evidence of trauma to the vagal or splanchnic nerves, although in Case 2 the patient had a total pneumonectomy and there may have been some imperceptible damage to these structures as they passed through the mediastinum. In the others there was no mechanical interference with the nerves for the operative sites were remote. Local vascular changes were apparently not a factor for in none of the cases was there thrombosis or sclerosis of the vessel walls even within the ulcer

beds. In Case 1 the vessels surrounding the ulcers likewise showed no appreciable changes.

The similarity between the surgical procedure in Case 1 and that used in producing peptic ulcers in dogs by McMaster is so striking that it cannot be passed over without comment. In 20 dogs he performed a simple jejunocecostomy and left undisturbed the portion of the gut between the anastomosis. Acute subacute or chronic peptic ulcers developed in 13 dogs, or 65 per cent. In 3 dogs there was spontaneous perforations and peritonitis. In another group of 11 dogs a jejunocecostomy was also performed but the intervening portion of bowels was resected. Only 2 of these dogs or 18 per cent developed peptic ulcers. In none of the dogs was the upper abdomen touched or traumatized in any way. The author stated that the mechanism involved in the formation of the ulcers was not divulged. In Case 1 several weeks passed between the time of the anastomosis and the resection of the short circuited loop. Whether this procedure had anything to do with the formation of the gastric ulcers is of course not known but the similarity between this case and the experiments on the dogs just referred to is most interesting.

SUMMARY

A review of the literature discloses very few reports on acute peptic ulcers following operation on other than the upper gastrointestinal tract. Five cases are presented here. One of these patients died from hemorrhage following erosion of an artery in the stomach wall. The remaining 4 ulcers were in the duodenum. One had perforated and produced peritonitis, another penetrated into the head of the pancreas and were limited by the muscle coats. The causes of the ulcers were not apparent.

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THE INTERNAL EPICONDYLAR EPIPHYSIS AND ELBOW INJURIES

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FRACTURE dislocation of the elbow in children with inclusion of the internal humeral epicondyle into the joint is not a frequent injury. It is not as rare, however, as was formerly believed. The injury is of extreme importance since the full significance of the pathology is not always appreciated. The dislocation is easily diagnosed, but the displacement of the internal epicondyle into the joint is often unrecognized; the dislocation is reduced but the epicondyle remains within the joint. As a result the child may be doomed to a markedly restricted painful range of motion in the elbow. Since these patients are usually treated first by the general practitioner, camp doctor or interne, it is highly important that they suspect and look for a displacement of the internal humeral epicondyle in every case of elbow dislocation in children. If a correct diagnosis is made early and the patient treated properly, a well functioning elbow with practically complete and painless motion will usually be insured.

Clinical examination gives some indication of the injury present. A dislocation is obvious and is easily recognized. The normal prominence of the internal humeral epicondyle should be looked

for and its absence noted. Comparison should be made with the opposite normal elbow. The presence of localized tenderness over the region of the epicondyle may be significant. Detailed roentgenograms in various views are essential to a correct diagnosis. Fluoroscopic examination alone is inadequate for recognition of the displaced ossicle.

In early cases, the dislocation and displacement of the epicondyle into the joint are both easily reduced by the closed method described in my previous reports. Clinical experience has shown that the method is so important in order to obtain a good result that a review of its description would not be amiss. Its mechanism depends upon the anatomical fact that the internal humeral epicondyle gives origin to a group of muscles by a common tendon. These muscles are the pronator teres, flexor carpi radialis, palmaris longus, flexor digitorum sublimis (humeral head) and the flexor carpi ulnaris (humeral head). By their action these muscles pronate the forearm, flex the wrist and fingers, and aid in flexing the elbow. It is evident, therefore, that if these movements are reversed, marked tension will be applied through these muscles to their point of origin, the epicondyle. With the epicondyle lying free within



Fig. Case a, July 4, 1930, separation of internal epicondylar epiphysis, with mild downward, medial and anterior displacement. b, August 7, 1930, slight improvement, with elbow in acute flexion.



Fig. 2. Case 2. a, May 31, 1930, posterior and lateral dislocation of right elbow without separation of epicondyle. b, June 20, 1930, twenty-nine days after closed reduction. Note bony proliferation from external condyle of humerus along lateral aspect of joint.

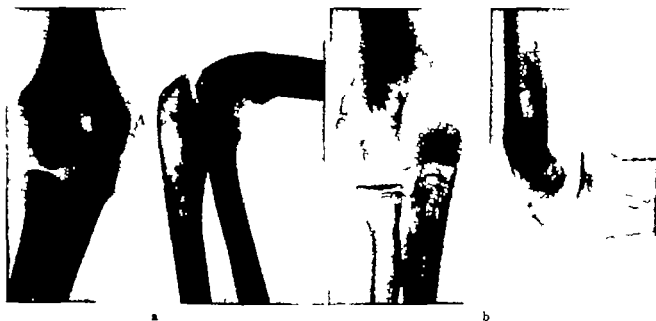


Fig. 3. Case 2. a, 5 months after injury. Note fragmentation at external humeral condyle as well as increased bone production from internal epicondyle. b, April 28, 1931, 23 months after injury. Note further fragmentation at external humeral condyle and increased bone production from internal epicondyle. Joint appears normal and function is complete.

the joint such tension upon it should dislodge it from the joint. The forearm is therefore, supinated and the elbow, wrist and fingers are extended. At the same time the forearm is gently abducted in order to increase the gap between the trochlea and the ulna, thus allowing the epicondyle a free route of exit from the joint. In every early case in which the author employed this maneuver the reduction was easy and complete. It is important to note that no force is required to effect the reduction. In late cases, however

where adhesions have already formed to bind the displaced epicondyle in the joint, open reduction will be necessary. The possibility of some resultant loss of motion is great in these latter cases. Hence the importance of early diagnosis and treatment. In all of the cases in my series except one reduction has been successfully carried out by the closed method. This latter patient was first seen 3 weeks after the reduction of the dislocation and is considered a late case. The encroachment of the internal epicondyle in the joint apparently was



Fig. 4. Case 3. a, November 7, '04, posterior and lateral dislocation of elbow of epitrochlea. b, Following closed reduction. c, Good reposition of epicondyle. d, Intra articular interposition.

not recognized originally. Open reduction was required to remove the epicondyle from the joint since it was too late even to attempt closed reduction.

The center of ossification of the internal humeral epicondyle appears at about the age of 5 years and fuses at about the age of 18 years. During this time there is always the possibility that the epicondyle may become avulsed generally by indirect trauma. The medial epicondyle gives attachment to the ulnar collateral ligament as well as to the superficial flexor muscles of the forearm. Excessive tension on these structures with the elbow in extreme valgus position may avulse the epicondyle or rupture the internal lateral ligament. Indirect violence such as a fall on the outstretched hand with the elbow extended is the history usually obtained. In some of my cases, however, there was a history of direct trauma with a definite fall on the elbow. The degree of pathology varies with the severity of trauma. In the least serious cases the medial epicondyle is only slightly separated. One such case is included in this series. When the trauma is more severe the epicondylar epiphysis may be pulled down to below the articular level of the elbow by flexor muscle pull. The internal lateral ligament and joint capsule may be strained or torn. With greater valgus strain it is possible for the elbow to open momentarily on its medial aspect so that the epicondyle becomes wedged in the joint between the trochlea and the sigmoid fossa of the ulna. Actually there is no dislocation of the elbow. Such cases have been described by

Watson-Jones. In the author's cases in which x ray films revealed similar wedging of the epicondyle he has always obtained a history of definite dislocation which was reduced without replacing the epicondyle. The resultant x ray films are similar to those of Watson Jones. When no attempt has been made to reduce the dislocation the roentgenograms reveal the dislocation as well as the epicondyle in the joint. The dislocation is generally lateral and posterior.

In these severe cases with elbow dislocation, the ulnar nerve may be stretched or actually carried into the joint with the displaced epicondylar epiphysis. In 1 case previously reported patient had a definite ulnar nerve paralysis which required open operation for neurolysis and anterior transposition of the nerve subsequent to successful closed reduction of the fracture dislocation. Ulnar nerve function was completely restored. In a second case previously reported there was presented a median nerve disturbance which recovered completely following closed reduction. In the cases to be described patients were devoid of any nerve involvement.

The epiphyseal plate connecting the internal epicondyle to the humerus is generally considered to be the weak link on the medial aspect of the elbow. Ordinarily a severe trauma will cause a disruption at this point. It is possible in some of the severe cases, however, to have a complete dislocation of the elbow without any displacement of the epicondyle. The extreme valgus tension on the inner aspect of the elbow in such a case produces a rupture of the ulnar collateral ligament



Fig. 5. Case 4. a, Complete separation of epitrochlea with displacement into elbow joint. Unrecognized at time of injury 3 weeks previously. b, 20 days following open reduction.

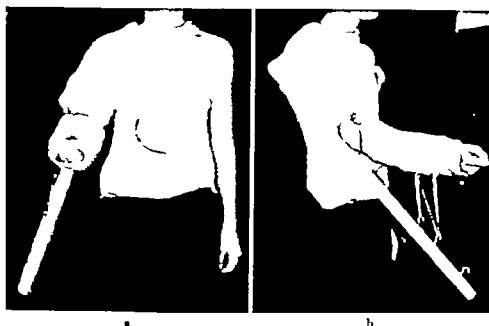


Fig. 6. Case 4. Plaster-of-Paris shoulder spica with extension piece for traction. Hinges incorporated at elbow for motion.

without disturbing the attachment of the epicondyle to the humerus. One such case is included in this series.

CASE 3. A colored boy of 9 years injured his left elbow during a fall on July 24, 1932. He was admitted to Sydenham Hospital where x-ray films revealed a mild separation of the internal epicondylar epiphysis with mesial, anterior and down and displacement. This case illustrates the simplest type of pathology. The elbow was immobilized in cut. Flexion with pronation of the forearm for 3 weeks. After only 2 weeks of physical therapy motion of the elbow was almost complete. The patient failed to return for further therapy, however.

CASE 4. A 10-year-old colored boy fell and injured his right elbow on May 3, 1939. He was brought to the

emergency room of Sydenham Hospital where clinical examination revealed an uncomplicated dislocation of the elbow with lateral and posterior displacement. All of the epiphyses appeared to be in normal position. In this case the ulnar collateral ligament was vulnerable whereas the internal epicondyle remained attached to the humerus. Reduction was obtained under general anesthesia, and the elbow was immobilized in flexion for 2 weeks. Physical therapy was instituted and the patient obtained practically a complete range of motion from 30 degrees of flexion with normal pronation and supination.

The roentgenograms dated June 20, 1939, almost 1 month after surgery reveal bony proliferation from the external condylar distally along the course of the external lateral ligament. This is a common finding in elbow dislocations and was present in both of my earlier cases. The



Fig. 7. Case 5. a, Anteroposterior and lateral ray films following closed reduction of dislocation of elbow. Note suspicious oval shadow in lateral view overlying olecranon process (thin the joint). b, With the elbow in greater extension, the internal humeral epicondyle is easily observed (thin the elbow joint).



Fig. 8. Case 5. a, Epitrochlear epiphysis in normal position following closed reduction. b, 36 days after closed reduction. Firm fibrous union of epicondylar epiphysis is present clinically.

later ray films, however reveal fragmentation of the region of the external condyle as well as bony proliferation from the internal epicondylar epiphysis. This condition has never been previously observed nor has the author been able to find any record of such finding in the literature. These changes evidently do not interfere with joint motion.

CASE 5. A colored boy, 6 years old, fell on his left elbow while playing basketball on November 7, 1941. He presented clinical and ray evidence of posterior and lateral dislocation of the elbow with inclusion of the separated internal humeral epicondyle into the joint. Complete reduction was obtained by the closed maneuver and the arm was immobilized in Velpeau dressing. The patient failed to respond for over a month, and elbow motion was definitely restricted. Physical therapy was immediately instituted and after three treatments elbow motion was possible from 75 degrees to 30 degrees. Pronation and supination were complete. The patient again disappeared. His failure to co-operate deprived us of the opportunity of giving him a complete, functioning elbow. It is probable, however, that he obtained this with normal activity.

CASE 6. A girl, 12 years old, as first seen in the dispensary of the Hospital for Joint Diseases on August 19, 1938. Three weeks previously she had tripped over a tent rope at camp and had struck her right elbow against the ground. X-ray films at camp had revealed dislocation of the elbow which was reduced. Since the elbow remained "frozen," she was brought to the city for further study.

Examination revealed a painful, enlarged elbow, fixed to 90 degrees neither flexion nor extension was possible. Pronation and supination were somewhat restricted. Roentgenograms revealed complete separation of the epitrochlear with displacement into the joint. A view of the lapse of time since the injury was sustained, it did not seem feasible to attempt closed reduction. Open operation was therefore performed on August 20. The epicondyle was found firmly bound down in the sigmoid fossa by scar tissue, and it was evident that closed reduction at this late stage could never have been successful. The epicondyle was gently freed and removed from the joint with its muscles. It was then sutured to the periosteum and an internal intermuscular septum just above the internal condyle of the humerus.

In view of the length of time that the epicondyle remained in the joint with its damage to the articular cartilage, it was feared that subsequent motion would be impaired. Even when the oleoid was removed on the operating table, the joint could not be carried through a normal arc. Despite every means postoperatively, elbow joint motion was only mildly improved. Physical therapy was first employed. A basswood gutter splint was then applied with gradual traction in order to increase elbow extension.

A two-sectioned tumbuckle plaster-of-Paris cast with hinges at the elbow was applied from the upper arm to the palm. A two-sectioned plaster-of-Paris shoulder spica was also applied with hinges at the elbow and an extension piece from the upper arm posteriorly. Hook screws were inserted into the forearm portion of the plaster as well as into the extension piece, and heavy rubber bands were applied between them for traction. Despite all these devices, only temporary improvement in joint motion was obtained and this could not be retained. Finally on March 22 x-ray films revealed narrowing of the joint space and it was evident that a normal range of motion was impossible. When last seen on April 19 the elbow could be flexed to 80 degrees and extended to 105 degrees. The failure originally to recognize the epicondyle in the joint and to reduce it early produced intra-articular changes which precluded satisfactory recovery of elbow motion.

CASE 5. A 10 year old boy fell on his left elbow while at camp on July 13, 1941. There was immediate deformity of the elbow which reduced itself spontaneously as the arm was being placed in a sling by the nurse. He was seen by me within an hour. Examination revealed marked tenderness over the internal epicondyle and as the forearm was gently abducted on the upper arm, the elbow redislocated. It was easily reduced. These findings indicated that we were either dealing with a rupture of the internal lateral ligament of the elbow or with a complete avulsion of the internal humeral epicondyle. Roentgenograms taken at Fairview Hospital appeared to be negative on casual inspection. More careful observation, however, revealed a faintly visible oval shadow superimposed on the olecranon in the lateral view. Because of the marked tenderness over the internal epicondylar region it was decided to take additional films with the elbow in greater extension. These films confirmed my suspicion and clearly revealed the internal epicondyle displaced within the joint. Under general anesthesia the displaced epicondyle was reduced out of the joint by the closed maneuver described. The elbow was immobilized in flexion and pronation, since

this position relaxes the involved muscles and avoids further tension on the epicondyle. The awareness of the possibility of a separation of the internal epicondyle with its inclusion into the joint, in cases of elbow dislocation, spared this boy the fate of the previous case. He obtained a complete range of arm motion at the elbow except for extension which was restricted less than 5 degrees.

EVALUATION OF STUDY

Avulsion of the internal humeral epicondyle may be simple or may accompany elbow dislocation. Conversely dislocation of the elbow may occur alone or be accompanied by a separation of the internal humeral epicondyle. In those cases of dislocation in which the epicondyle becomes displaced within the joint it is highly important that the entire pathology be recognized early and treated without delay. Complete reduction can be obtained in those cases that are treated early by the closed method described. The maximum length of time following injury in which closed reduction may be successful cannot be stated with accuracy. All of the patients in the author's series in which the dislocations were successfully reduced by the closed method were treated within 24 hours after injury. All of them obtained well functioning painless elbows. In the 1 patient who came to open reduction the condition was not accurately diagnosed until 3 weeks after injury. It was too late then to attempt a closed reduction. The relatively poor result obtained in this case emphasizes the extreme importance of early accurate diagnosis and treatment.

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REPARATIVE PLASTIC SURGERY OF SECONDARY CLEFT LIP AND NASAL DEFORMITIES

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THE stigma of a harelip facies may remain following the initial surgery. Though the latter has been adequate the deformity may be unsatisfactory because of inherent defects present both in the lip and nose. With this in mind a definite plan must be outlined before any operative work is begun and such a plan must cover a span of years (Fig. 1). When secondary repair is considered then the method and the time should be planned when the primary closure is carried out.

The nasal deformity as well as that of the lip identifies the harelip patient. Unless the lip is grossly too long or too tight complicating secondary surgical repair a reasonable reconstruction may be expected. However unless the nose too is reconstructed the final picture will be found wanting. The surgeon must weigh the future when proceeding with a primary repair and when possible avoid external incisions on the nose. Tissue may be readjusted to allow for a reasonable result with the thought that the procedure may be adequately completed at some later time (9).

PLANNING RECONSTRUCTION OF THE PRIMARY HARELIP

The plan must include the necessity and timing of any future surgery either of the lip itself or of the deformed nose. If the defect is associated with a cleft palate and the latter is continued anteriorly including the premaxilla then the technique must be further modified (). Time and later orthodontia will do much to approximate even wide alveolar clefts. Forceful wiring of the maxilla will often result in irreparable malformation and loss of teeth (4, 14). Occasionally in primary repair a wire may be introduced between the two separated halves of the maxilla entering it high on either side and making certain that it is not too tight. It is applied in especially wide clefts and allowed to remain 3 to 6 weeks.

Many pitfalls are offered by the double harelip especially one with a prominent or a floating premaxilla. A carefully planned operation with un-

dermining and advancement of the cheek after it is freed from the alveolar process of the maxilla will result in reasonable occlusion (2). When the premaxilla has been sacrificed at primary closure, the result is usually unhappy; the upper lip is short, tight and markedly retruded.

Much discussion has accrued whether the skin of the probrium is part of the lip or columella. Brown and McDowell (3) have pointed out that the skin borrowed from the probrium to create the columella in cases of bilateral harelip usually grows hair and so it would appear to be part of the lip.

The initial closure should seek to gain a symmetrical nose with nostrils and a columella that will lend themselves to future surgery and a lip that is neither too short, long or tight.

A prominent deformity that may occur with double harelip is a short columella. To overcome this defect cartilage may be implanted at the primary operation so as to stretch the columella. At the time of secondary repair more cartilage is often inserted as a strut running from the nasal spine to the tip. In those cases in which the lack of columella is such that it may not be remedied by stretching then a small rectangular flap is turned from the center of the philtrum at its juncture with the columella and slid upward to join the latter.

PRINCIPLES IN THE TECHNIQUE OF PRIMARY REPAIR

Regardless of the method of procedure, definite accomplishments are desired at the time of primary closure. Brown and McDowell (3) have succinctly expressed these principles. To gain (1) a pleasing alar direction and level, (2) an intact nostril floor, (3) a symmetrical lip, (4) a straight columella, (5) the upper lip prominent in advance of the lower lip and a full vermilion border, (6) if possible a cupid's bow upper lip and the suggestion of a philtrum.

These accomplishments are not easily acquired but unless they are considered they rarely occur spontaneously. In conjunction with careful pre-operative planning the surgeon must be prepared to make his surgical method elastic to meet the problems as they arise at the operating table.

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Presented in abbreviated form in conjunction with colored surgical motion pictures at the Santa Barbara County Medical Association, May 1944.



Fig. Primary harelip and cleft palate repair. a, The flattened nostril, the misplaced vermillion border and the flaring short side are well depicted. b, The area to be undermined and the points to be approximated are demonstrated. The lower lateral cartilage is undermined both on

its anterior and posterior surfaces to allow it to slide into position. c, The flaring prelabium on the affected side is seen. d, The associated cleft palate with a prealveolar cleft complicates the case. e, Photograph 3½ years following repair of the palate, lip, and nose.

Preoperative study. Photographs are taken of the child both for study and record. Front view, profile, and nasal triangle shots are important to gauge the amount of deformity. When there is an associated cleft palate, a camera is used with the lens at F40 to gain a closer focal distance.

Calibration and marking. The projected lines of incision are marked with a 3 per cent gentian violet solution (U.S.P.). The points to be approximated are carefully measured with calipers so as to obtain a lip that is neither too long nor too tight (Figs. 17-18-10).

When the nasal floor requires reconstruction, then sufficient tissue is allotted from the affected side, turned upward, and sewn into position.

The measurements, planning and judgment are more difficult than the surgery. As little tissue as possible should be sacrificed. Compensation must be made for contracture and growth, often a reasonable result at the operating table appears quite different and possibly disappointing several years later.

Undermining. Not only should the whole cheek on the affected short side be undermined away from the alveolar process of the maxilla but so too should most of the cheek on the opposite side (Figs. 15-16).

Through the gingival margin on the affected side the whole lateral crus of the lower lateral cartilage is meticulously undermined on both its



Fig. Secondary repair. a, The overhanging ala and flattened nostril on the affected side are typical of this deformity. b, Following repair the nose shows a more pleasing nasal triangle. c, Retraction of the lip and prominent lower lip mark this patient as a "barelip." d, The plaster cast is used as a model for preoperative study. e, Reconstruction of the nose with cartilage grafts and reconstruction of the lip with an insertion of dermal graft has helped to overcome the deformity.

anterior and posterior surfaces. The undermining anteriorly is high and includes the lower aspect of the upper lateral cartilages especially on the affected side and should extend past the midline (Fig. 4). There is a definite distortion of the lower lateral cartilage present and unless it is freed and allowed to slide the contour of the nostril will remain distorted and buckled at an angle when an attempt is made to bring the affected nostril up to position.

The angle of the ala should be overcorrected. Allowance must be made for contracture and

growth. Several mattress sutures are passed through the skin, cartilage and nasal lining after the lower lateral cartilage has been undermined. This fixes the distorted cartilage to its new position and helps to avoid bleeding and hematoma.

Sutures. Fine white silk is employed to approximate the muscles, for it is believed that silk is stronger than catgut results in less induration and allows for earlier symmetrical movement of the whole orbicularis oris.

To avoid the telltale suture marks on the lip the skin is approximated with a subcuticular silk



Fig. 3. Illustrating the surgical method in repair of secondary lip deformities. a The scar is followed to locate the lip. Relaxing incisions (after J. B. Brown) may

be used along the alveolar margin to gain tissue. b The necessary tissue has been excised and readjusted. c, The mucous membrane has been approximated.

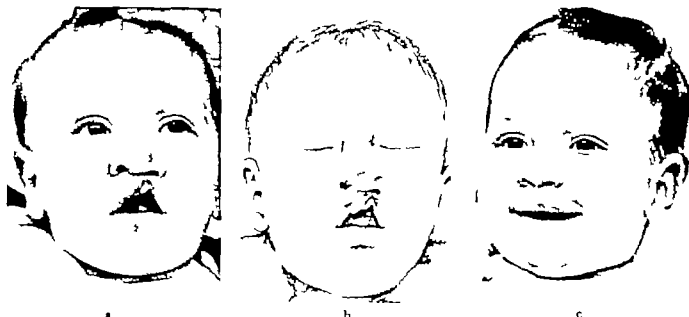


Fig. 4. Primary repair. a, The fullness on the short side must be utilized to gain a symmetrical lip. b Reconstruction of the nostril is a prime requisite in harelip repair. The

lines of incision and area of undermining are demonstrated. c, Photograph showing the result which was secured following surgery.

suture and the latter is removed in a week or 10 days.

RECONSTRUCTION OF SECONDARY DEFORMITIES

Preoperative study. A plaster mask is taken of the face from which meticulous measurements are made both of the lip and nose. When required the nasal deformity may be reconstructed with modeling clay so as to gain a more exact plan of the surgical approach. The photographs taken of the front view, profiles and triangle of the nose are conjointly helpful (Fig. 2). When cartilage implants are required their measurements may be taken from the plaster cast and modeled to fit the deformity.

Deformities confronted in secondary repair of a harelip are the following:

1. The upper lip is short and tight resulting in malocclusion of the teeth. This is usually associated with a protruding overhanging lower lip. A cleft prealveolar process or a surgically absent premaxilla may cause further complication in the picture.

2. The lip may be long and narrow.

3. The vermillion border may be asymmetrical, notched and partly extending into the upper lip proper.

4. Wide suture marks producing a telltale ladder deformity across the lip.

5. The nasal ala on the affected side is low.



Fig. 5 Necrocartilage fixed directly in Bouin's solution $\times 30$. This photomicrograph reveals well preserved cartilage with the cells and nuclei appearing normal. In a few places the cells are vacuolated. The matrix immediately around the cells is deeply blue stained, but elsewhere it is pink.

flattened and enters the cheek at a right angle rather than a curve. The opposite nostril is usually flaring.

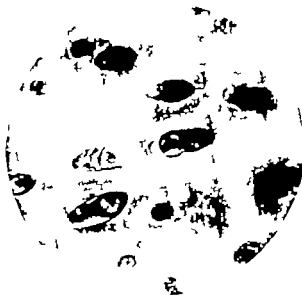
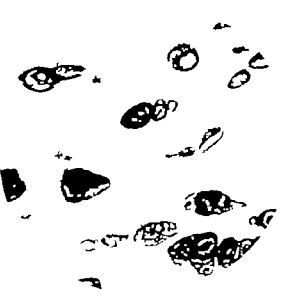


Fig. 7 a. Necrocartilage placed in anterior abdominal wall 6 months, then removed and fixed in Bouin's solution. The cartilage is well preserved. The nuclei are distinct. In some places the cells are vacuolated. At the periphery the stain is pink and there is moderate dissolution of the nuclei



Fig. 6 Necrocartilage placed beneath anterior abdominal wall 6 months, then removed, and fixed in Bouin's solution $\times 30$. Cells in center are large and blue stained, in places, vacuolated. Nuclei are prominent. Matrix shows unusual light and dark blue. At periphery tissue is diffusely pink stained, moderate dissolution of cartilage cells.

6 The upper lateral cartilage on the affected side is flattened and there is a flare of the nasal lining into the vestibule.



and cells. b. Necrocartilage refrigerated in merthiolate-saline solution 4 for 6 months, then fixed in Bouin's solution $\times 30$. This presents almost an identical microscopic picture throughout as the cartilage stored in the abdominal wall (Fig. 7a).



Fig. 8. a, Autogenous cartilage stored in the abdominal wall 9 months, then removed and fixed in Bouin's solution. Histological comparison reveals this cartilage to appear not much different than necrocartilage treated identically. While most cellular and nuclear outlines are clear, there is a moderate dissolution of cellular elements at the periphery.

7. The columella may be short, malformed or disappearing.

Many of these deformities are unavoidable and must be surgically ignored until the appropriate

time for their repair. Procedures which are momentarily spectacular may produce a defective end result (20).

Surgery. The anesthetic is usually local com-



Fig. 9. a, b, Necrocartilage stored in the anterior abdominal wall 2 1/2 years, then removed and fixed in Bouin's solution. Low and high magnification. The cells at the

center are reasonably well preserved. The matrix is mainly pink stained. There is an area of focal necrosis in the center.

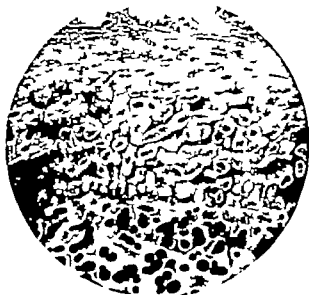
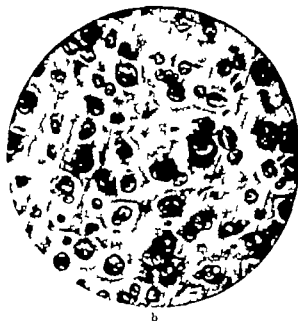


Fig. a, Low and b, $\times 30$, necrocartilage refrigerated in merthiolate saline solution for 14 years. This specimen is fairly well preserved compared to the previous one.



The matrix appears lavender and closely resembles histologically the fresh necrocartilage, which is illustrated in Figure 5.

binning nerve block and infiltration. When general anesthesia is necessary, intratracheal is preferred. The operation may be performed in one or two

stages, the nasal reconstruction usually first.

The peculiar deformity of the nose, especially the nasal triangle, as well as the lip defect calls attention to the harelip patient. A complete rhinoplastic operation is therefore carried out with special attention paid to the tip. The lower lateral cartilages are dissected free. On the affected side, the nostril is usually smaller so the lower lateral cartilage is severed at the arch, the lateral crus completely undermined and allowed to slide. Often a section of cartilage taken from the opposite ala is inserted within this gap. On the unaffected side a similar procedure is done, but here the required amount of cartilage is removed to create less flare and a smaller nostril. The cartilage of the unaffected nostril may be severed more laterally with the remaining medial wing then bent toward the opposite nostril to gain support.

The lower lateral cartilages are dissected free without removing nasal lining. When there is an overhanging nostril or a notch in the ala, the lining is undermined down to the edge of the ala and adjusted to approximate the new position and shape of the lower lateral cartilages.

THE USE OF NECROCARILAGE

Few harelip noses are reconstructed that do not require cartilaginous struts either on the dorsum, in the columella, at the columellar philtrum junction and occasionally along the alar margins (6

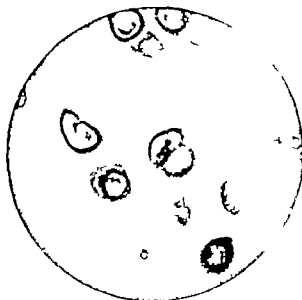


Fig. c. Autogenous cartilage stored in the anterior abdominal wall 14 years, then removed and fixed in Bouin solution. The cartilage presents striking alteration from the normal. There are irregular areas of degeneration characterized by loss of nuclei and cellular structures and diffuse pink cast to the matrix. It soony says it closely resembles the necrocartilage stored in the abdominal wall for 14 years.



Fig. 12 Secondary harelip and nasal repair. a, left Overhanging flattened ala with a notched lip and vermilion border b Complete rhino-osteoplasty and reconstruction of the lip

18 19 21) (Fig. 14) We have been using rib necrocartilage fixed first in 4 per cent formalin then refrigerated in merthiolate solution (17)

Experimental work in grafting a whole ear necrocartilage (cadaver) has been continued with rib necrocartilage implanted intranasally (11, 12 13) To follow the histopathological course of the grafted specimens, portions of the same cartilage

were implanted in pockets beneath the anterior abdominal wall (15 22) Then in intervals after the first week, month 6 months 12 months and 30 months sections were removed for microscopic study (Figs. 5 through 10) Concurrently other pieces of the same rib necrocartilage were continued on in merthiolate saline solution and examined for comparison after the same time in

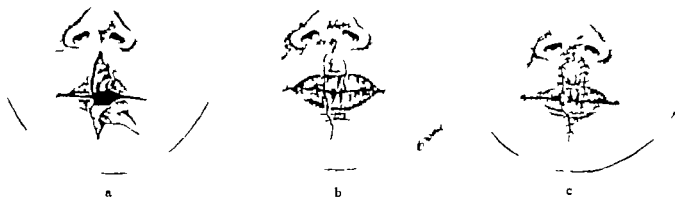


Fig. 13. Illustrating the Eastlander Abbe flap. a A full thickness triangular section of lower lip with the left inferior labial artery attached is dissected free. b An incision is made through the upper lip and the pedicle with its artery attached is turned into position c, The lower lip is

closed and the wound edges of the upper lip are approximated to the pedicle. Two to 3 weeks subsequently the inferior labial artery is severed at which time the pedicle which was turned into position has gained total circulation from its new residence.

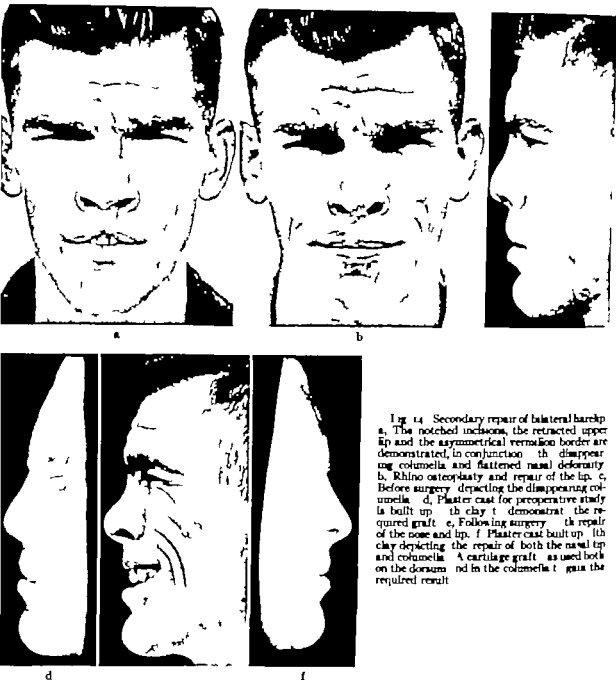


Fig. 14. Secondary repair of bilateral harelip. a, The notched incisions, the retracted upper lip and the asymmetrical vermillion border are demonstrated, in conjunction with disappearing columella and flattened nasal deformity. b, Rhino osteoplasty and repair of the lip. c, Before surgery depicting the disappearing columella. d, Plaster cast for preoperative study is built up with clay to demonstrate the required graft. e, Following surgery the repair of the nose and lip. f, Plaster cast built up with clay depicting the repair of both the nasal tip and columella. A cartilage graft was used both on the dorsum and in the columella to gain the required result.

intervals. Further this rib necrocartilage was microscopically compared with autogenous cartilage under similar circumstances (Fig. 11).

After the first week, the cartilage implants showed some local foreign body reaction in the circumscribed tissue. The cartilage itself was intact but for slight dissolution of the cells around the periphery. After 6 weeks, the surrounding tissue showed little local reaction and the cartilage it

self presented well preserved cells with distinct nuclei. The matrix stained blue throughout and at the periphery took up a pink stain. After 6 months the microscopic picture varied little from the previous one except that the periphery presented a slight dissolution of nuclei and cells. At the end of 2½ years a previously measured specimen was removed and it was found that the dimensions and gross consistency had not changed.



Fig. 15a.



Fig. 15b.



Fig. 15c.



Fig. 16a.



Fig. 16b.



Fig. 16c.

Fig. 15 Primary harelip repair. a The flattened ala, the deformity of the lip and vermilion border are of primary concern. b The lines of incision, the points of approximation and the area to be undermined are depicted. Careful planning of the operation and the future course are prime requisites. c, Following reconstruction. Further surgery on the nose may be postponed until the child approaches adolescence at which time a total rhino-osteoplasty may be done.

Fig. 6 Primary harelip repair. a Fullness of the lip on the short side. Cognizance of the picture is important and tissue must be utilized and adjusted to gain desired result. b The incision on short side is carried lateral to alar attachment. The floor of nose is required to compare with opposite side. c, Following surgery.

Fig. 17 a, b, Primary harelip. The lip and nasal deformity have occurred in conjunction with a complete unilateral cleft palate. The anterior floor of the nose is re-



Fig. 17a.



Fig. 17b.

constructed by gaining a triangular flap from the short side. Thorough undermining of both cheek as well as the affected nasal ala past the midline is most important.



Fig. 8a



Fig. 8b



Fig. 9a



Fig. 9b



Fig. 10

Fig. 8 a, b Primary harelip. Though this is an incomplete left, it is presented to emphasize that the lines of incision must be carried to the floor of the nose and that the latter along with the nasal ala must be surgically adjusted in order to obtain the desired result.

Fig. 9 a, b Primary harelip repair. The lines of incision and areas to be undermined are illustrated. The flaring short side requires that point be placed lateral to the left alar attachment in this manner reconstructing the

deformity so that it will compare with the opposite side.

Fig. 10 Secondary harelip and cleft palate. This patient, aged 24, had several operations in childhood. In one the premaxilla and a good portion of the soft palate were removed. Because of the former absence, the whole palate has contracted, the premolars are anterior and the upper lip is markedly retruded. In spite of the short, tight palate, the patient presents quite good enunciation because of speech training.

Most of the matrix stained pink and the cells at the periphery were less well preserved than those in the center. The periphery also presented several areas of focal necrosis.

Comparatively for the first several months the identical cartilage kept in solution was hardly discernible microscopically from that implanted in the body. The section examined after 1 year shows the necrocartilage retained in solution better preserved than that implanted in the anterior abdominal wall. However the implant of necrocartilage when compared with an implant of autogenous cartilage buried for the same length of

time shows little relative difference. Both present some dissolution of the architecture of the cartilage at the periphery and similar change of the cellular and nuclear structure. Grossly the two pieces hardly differed when compared.

Clinically as long as 3 years afterward, the intranasal necrocartilage implants appear intact and responsible. In no case did we meet with infection or drainage. All healed primarily and their clinical course from the standpoint of induration, redness, tenderness, etc. was no different than our experience with autogenous cartilage transplants. Our series of necrocartilage transplants that have

been followed both clinically and microscopically number 62

Preparation of the necrocartilage implants The necrocartilage grafts are prepared several days before surgery. Both the patient and the cast are used as a model and the specimen is first sculptured grossly with the scalpel. Then the electric burr and fine sandpaper are employed to gain exact size, contour and smoothness. Several small holes are made in the prepared cartilage to allow granulation tissue to push through to hold it in place.

The cartilage is then cleansed and returned to the refrigerator in merthiolate solution. When the graft is implanted at the operating table it may be sprinkled with sulfanilamide crystals to aid both in asepsis and fibrosis.

SURGERY OF THE LIP

The lines of incision are carefully marked with three per cent gentian violet solution. The opposite side is used as a criterion in repairing the affected side. As much as possible of the old scar or notching is removed without creating a lip that is too long or tight. Incisions are carried along the alveolar margins on both sides and the cheeks are freed from the maxilla (Fig. 3). The former are undetermined, allowing the lip to advance toward the center. Incisions are made through the full thickness of lip the necessary amount of scar is removed and the floor of the nose and muscles of the lip are approximated with buried fine white silk (Fig. 12).

A subcuticular suture is employed to avoid the ladder scars and a few fine silk sutures are placed in the skin and removed early. The vermillion border is interdigitated in the shape of a 'V' forward on one side and reverse on the other. A Bowman's splint is applied and the diet is fluid for several days.

In those patients with a short retruded lip after having gained tissue from either cheek we may insert cartilage within the lip extending from ala to ala under the nose and down to the vermillion border. Because these patients have previously used the upper lip but little for speech the cartilage within the lip is not an inconvenience. The lip is thrust outward causing it to stretch so that time improves the result.

Pedicle flaps from the lower lip The vermillion border flap from the lower lip (Eastlander or Abbe flap) with the inferior labial artery intact and attached on one side has often been used (5). Though the transfer may be satisfactory in expert hands, the resultant scar both on the lower and upper lip and the possible difference in color

of the flap with the passage of time has made us feel that its employment is limited. We consider its use in patients with bilateral harelip in whom the prolabium has unfortunately been discarded at some previous operation. Often in such cases the lower lip is markedly prominent and giving up some of its tissue improves the cosmetic appearance (Fig. 13).

Dermal grafts These grafts are easily obtained especially with the use of the Padgett dermatome. The thick split skin graft is cut first then the required derma is dissected free as one does a full thickness graft. A pocket is created within the upper lip preferably through the old scar and the dermal graft is inserted. Sulfanilamide crystals are sprinkled over the graft previous to its implantation. The presence of the graft allows for prominence of the lip and is especially applicable for those cases of upper lip retrusion with scarring and fibrosis.

Lyndon Peer (16) followed the fate of full thickness grafts transplanted beneath the thoracic skin of humans. His conclusions indicated that the sebaceous glands do not survive transplant and further that no cyst formation occurred after 28 months. We have since repeated his work and verified his results.

Vermilion border In most cases there is both asymmetry and disappearance of the vermillion border. Women may employ lipstick to create an illusion, men, however are limited with cosmetic applications. The border may be reconstructed by removing the required amount of skin and vermillion lip undermining the latter and suturing it to its new position. Adjusting or sliding the mucous membrane may often be necessary to gain the required result (8).

TIME TO OPERATE IN SECONDARY PROCEDURES

Secondary procedures on harelip deformities may be performed at any age. As a rule we wait until the patient has passed adolescence before a complete rhinoplastic operation is performed (1). Depending upon the individual patient the extent of the deformity and the psychic affect it has produced may influence the surgeon to operate at an earlier age. It is our experience that rhinoplasty may be done when the patient is 7 or 8 years of age without deleterious effects. Care must be taken that there is no injury to the vomer during the process of straightening or adjusting the septum.

PROSTHESIS AND ASSOCIATED CLEFT PALATE DEFORMITIES

Often a patient with an anterior cleft or markedly deformed palate partially edentulous re-

quires a prosthesis. Working in conjunction with a trained dentist, the surgeon may construct the prosthesis to give the upper lip some support and protrusion without its being cumbersome and uncomfortable to the patient (10).

All patients who have had a cleft palate repair must be urged to undergo speech training for defective enunciation. Though a good secondary lip repair may be accomplished a patient with the telltale palate speech will gain less of a psychological improvement than if his speech were helped. Many patients with cleft palate speech are not conscious of the extent of their speech impediment, so that self improvement is virtually impossible and they must seek the services of a teacher.

Patients with a short tight palate and most with the soft palate missing may have good speech and are able to project the hard consonants, whereas other patients with a reasonably good palate are speech cripples (Fig. 20). Too often these patients are reoperated upon thus producing a better palate but no improvement in speech. In these patients speech training should be tried first and surgery reserved with judgment.

SUMMARY

1. Surgical principles in repair of secondary harelip deformities have been evaluated.
2. The importance of rhino-osteoplasty in secondary repair has been emphasized.
3. Necrocartilage has been followed experimentally and clinically in 62 cases and its use in these deformities judged.

4. The use of dermal grafts has been pointed out.

5. Prostheses are important adjuncts in harelip repair.

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AN EVALUATION OF THE CLINICAL SIGNIFICANCE OF SERUM AMYLASE AND LIPASE DETERMINATIONS

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ALTHOUGH a number of studies have been made of the significance of serum amylase and lipase in pancreatic disease more information is needed in regard to the relative diagnostic value of the two procedures. In 1929 Elman, Arneson and Graham reviewed the literature dealing with the value of serum amylase determination in pancreatitis, and more recently Lewison has presented a review of the subject. The study of serum lipase in connection with pancreatic disease was stimulated in this country by Crandall and Cherry. Comfort and Osterberg (3) have presented unequivocal evidence of its value in pancreatic disease in several papers. Johnson and Bockus (10, 11) have reviewed the status of the determination of this enzyme as an aid in diagnosis.

It is the purpose of this paper to compare and contrast the two procedures in the diagnosis of acute pancreatitis as well as in certain other upper abdominal disorders. One hundred and twenty-two consecutive serum amylase determinations in 104 patients and 165 consecutive serum lipase determinations in 135 patients provide the basis for this study. In 61 cases both enzyme tests were performed.

METHODS

Serum lipase was determined by the method of Crandall and Cherry.¹ Serum amylase was determined by the method of Somogyi (15) modified by substitution of the Folin (7) blood sugar method for the Shaffer-Hartman-Somogyi method. The modified method gives somewhat lower results than the original due to the greater specificity of the Folin reagent. Split products of amylolytic digestion affect the reagent employed by Somogyi to a much greater extent than does that of Folin causing the former to give higher results. Results are expressed as reducing substances (in terms of glucose) liberated per 100 cubic centimeters of serum. Lipase values are expressed as the cubic centimeters of one-twentieth normal sodium hy-

droxide required to neutralize the fatty acid liberated by 1 cubic centimeter of serum from the olive oil substrate during 24 hour incubation at 38 degrees C.

NORMAL VALUES

Our experience leads us to believe with Comfort that serum lipase does not normally exceed 15 cubic centimeters of twentieth normal sodium hydroxide per cubic centimeter of serum.

In a previous study (14) the normal range of serum amylase when the modified Somogyi method was used was found to be 62 milligrams per 100 cubic centimeters with a standard deviation of 13 milligrams. The normal limits thus were 36 milligrams to 88 milligrams (mean plus or minus twice the standard deviation). Because these figures differed appreciably from those mentioned by Somogyi as normal (80 to 180 mgm. per 100 c.c.) a second series of controls was examined as part of the present study. The results are shown in Figure 1. Here, the mean value is 61 milligrams and the standard deviation 19 milligrams making the normal range 23 to 99 milligrams. The results obtained by Somogyi differ from the preceding less than these figures would indicate, since he rejected a number of normal values below 80 milligrams without any apparent statistically sound reason. Therefore, combining our two series of controls, we have in this paper considered as abnormal serum amylase values over 100 milligrams and less than 30 milligrams.

DISEASES OF THE PANCREAS

In Table I it will be seen that 12 of 13 cases of acute pancreatitis showed serum lipase values over 15 cubic centimeters. All of the 9 cases in the amylase series had values over 100 milligrams per 100 cubic centimeters, and 8 of the 9 showed values over 200 milligrams. This is in accord with the results of other authors. Fifty five percent of the diagnoses in this group were proved by autopsy or operation. The patient who exhibited a normal lipase value (12 cubic centimeters) had an elevated serum amylase of 206 milligrams. This patient did not enter the hospital until several weeks after the onset of symptoms. It is of interest therefore, that the high serum enzyme activity persisted since several authors have shown that

With the technical assistance of George R. Kingsley, M.S. and Eleanor Fortunato.

This contribution was prepared from the wards and Division of Biochemistry, The Philadelphia General Hospital.

In determination of serum lipase, buffer solution was omitted since it was found that the absence of the buffer recommended did not influence results appreciably.

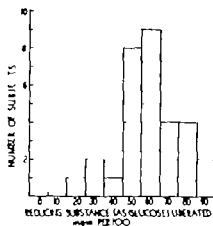


Fig. 1. Serum amylase in normal subjects. Dotted lines, present group; solid lines, combined group—data of Riggs and associates included.

the serum enzyme rise reaches its peak in about 72 hours and thereafter declines quite rapidly.

Serum amylase determinations were done in 7 cases and serum lipase in 16 cases of carcinoma of the head of the pancreas. Four of the amylase group and 12 of the lipase group had the diagnosis proved at either operation or autopsy. Only 1 of the 7 cases in the amylase series showed an elevation, while 9 of the lipase values had titres over 1.5 cubic centimeters. Wakefield, McCaughan, and McVicar found high amylase values in 6 of their 20 cases, but others have found a lower proportion of elevated values. Lewison's recent results are quite comparable with ours in that he found an elevated serum amylase in but 1 of 9 cases. On the other hand, using the lipase test, Comfort and Osterberg (3) in their series of 60 cases of carcinoma of the head of the pancreas found 40.5 per cent elevated. In this same group the amylase was elevated in only 2 of 24 cases. It is seen from these figures that serum lipase is affected more than serum amylase in cases of carcinoma of the head of the pancreas. Greater significance, however, should be attached to the fact that high lipase together with normal amylase, particularly in the presence of painless jaundice, is frequently associated with this condition and strongly suggests such a diagnosis.

In a group of miscellaneous diseases of the pancreas, 1 case of pancreatic calculosis with diabetes mellitus showed an elevated serum lipase of 2.3 cubic centimeters. Three of 5 cases in the amylase series had values over 100 milligrams. These were cases of pancreatic abscess (125 mgm.), pancreatic cyst (180 mgm.) and metastatic carcinoma from the breast (331 mgm.).

The total figures in all diseases of the pancreas

as seen in Table I show that 58 per cent of the 38 cases in the lipase group and 52 per cent of the 21 cases in the amylase group had elevated values.

DISEASES OF THE LIVER

Of the 10 cases of portal cirrhosis of the liver in the amylase series (Table II) all had values below 100 milligrams. Six of these were under 50 milligrams, and 4 were below 30 milligrams. In a group of cases without demonstrable liver disease (Table IV) only 3 per cent had a serum amylase under 30 milligrams. In the lipase series the same number of cases of portal cirrhosis show a more variable distribution of values although none exceeded a titer of 1.5 cubic centimeters. Thirty per cent of these were 0.3 cubic centimeter or less. However, the fact that the group of cases without any sign of liver disease (Table IV) also showed 30 per cent of the lipase determinations to be 0.3 cubic centimeter or below indicates that low lipase activity is not necessarily significant in hepatic disease.

Only 3 cases of primary liver neoplasm were encountered; none had elevated values and 1 had a serum amylase below 30 milligrams.

Thirteen cases of acute hepatitis (this classification includes all cases of infectious jaundice and acute toxic jaundice) are included in the lipase series, and 8 cases in the amylase series. Only one had an elevated enzyme value (lipase 1.6 c.c.). This case presented a clinical course typical of catarrhal jaundice and recovered completely. Two of the amylase values were below 30 milligrams.

Johnson and Bockus (10) found no lipase titration over 1.0 cubic centimeter in 15 cases of catarrhal jaundice and 2 cases of toxic infectious hepatitis. Foged found no elevations in 28 cases of acute hepatitis. Therefore our results agree with the findings of these workers.

Eight cases of miscellaneous liver diseases are presented in Table II. These included 2 cases of Hanot's hypertrophic biliary cirrhosis, 4 cases of metastatic malignancy and 2 of liver abscess. There were no values over 1.0 cubic centimeter for lipase or over 100 milligrams for amylase, while 2 of the 5 amylase figures were under 30 milligrams.

In all types of liver disease, low amylase activity was prevalent, and 26 per cent of the total were under 30 milligrams. Only 1 patient showed an elevated amylase activity.

GALL BLADDER DISEASE

Included in our investigation were 16 cases of chronic calculous cholecystitis in the lipase group, 9 with common duct stones, and 17 cases in the amylase group, 6 with common duct stones. There

TABLE I.—SERUM AMYLASE AND LIPASE IN DISEASE OF THE PANCREAS

Pancreatic disease	Lipase							Amylase						
	Total cases	c.N/30 NaOH						Total cases	Mgms. glucose liberated/ 100 c.c.					
		0-0.5	0.5-1	1-2	2-5	5-10	Over 10		Below 30	30-50	51-100	101-500	Over 500	
		Per cent of total							Per cent of total					
Pancreatitis, acute	3				8	9	9						80	
Carcinoma of head of pancreas	6		0			57	7	43	43				14	
Other diseases	9	45					5	20	20	20			40	
Total	18		8		3	58	11	5	4	0	20		5	

is a quite uniform distribution in both groups throughout the normal range, and only 3 cases in each series showed a markedly increased activity. Thus, in the lipase series, 3 of the group showed elevation and all of these had common duct stones. In the amylase series 3 patients had values over 200 milligrams and 5 patients showed enzyme activity between 100 milligrams and 200 milligrams. Three of the 6 cases in this series who had demonstrable common duct calculi had elevated values.

Not only did the 3 patients with elevated lipase values and the 3 with amylase activity exceeding 200 milligrams have calculous common duct obstruction but 4 also had demonstrable pancreatic involvement. One had a typical acute pancreatitis with widespread fat necrosis and 3 showed some pancreatic induration grossly or definite pathologic changes microscopically. In the other 2 the pancreas was not examined at operation. Likewise the pancreas was not examined in those patients of the amylase group with values of 100 milligrams, either because of the patient's refusal to undergo operation or because of some technical difficulty during the operation. The 3 patients presenting normal amylase values with stone in

the common duct showed no pancreatic involvement. Of the 6 with normal lipase values and calculous common duct obstruction 5 showed the pancreas to be normal and 1 showed some perenchymatous change of the organ microscopically. In the latter both enzyme tests were done one day after the onset of symptoms. The lipase titration was 0.6 cubic centimeter of one twentieth normal sodium hydroxide but the serum amylase was 244 milligrams. Thus, again as indicated in the pancreatic disease group (Table I) the advantage of performing both of the enzyme tests is unmistakable.

Thirteen cases of acute cholecystitis were studied none had increased enzyme activity but 2 of the 6 cases of the amylase series had values below 30 milligrams. One of the 5 cases of chronic cholecystitis without stones, in the lipase series, had an elevated value of 2.2 cubic centimeters the pancreas was not examined at operation however. Again, a single low amylase value was encountered in this group. There were 9 cases of carcinoma of the gall bladder or extrahepatic bile ducts without increased enzyme activity however 3 of the 4 cases in the amylase series had values less than 30 milligrams.

TABLE II.—SERUM AMYLASE AND LIPASE IN DISEASE OF THE LIVER

Liver disease	Lipase							Amylase						
	Total cases	c.c. N/30 NaOH						Total cases	Mgms glucose liberated/100 c.c.					
		0-0.5	1-0.5	5-10	10-50	Over 50	Below 30		30-50	51-100	101-500	Over 500		
Per cent of total						Per cent of total								
Cirrhosis		30	30		40			40	30	40				
Liver neoplasms				100				50		50				
Acute hepatitis	3	8	33	33	8	8	8	5		63				
Other diseases	3	67		33			5	40	40	80				
Total	17		33	30	8	4	5	35	6	44		4		

TABLE III.—SERUM AMYLASE AND LIPASE IN DISEASE OF THE GALL BLADDER

Gall bladder disease	Lipase						Amylase						
	Total cases	M/100 NaOH					Total cases	Mgms glucose liberated/100					
		0-10	10-20	20-30	30-40	Over 40		Below 30	30-50	50-100	100-150	150-200	Over 200
		Per cent of total						Per cent of total					
Acute cholecystitis	7	29	29	3	30		6	15	50	17			
Chronic cholecystitis	5	20	20	40		20		20		20			
Chronic calculous cholecystitis, with and without stone in common duct	16	25		5			7	6	2		4	6	13
Neoplasms—gall bladder and bile ducts			40	20	40			75		5			
Total	3		1	11	9		20	3	35	7	20	3	20

The combined figures for all diseases of the gall bladder as seen in Table III showed elevated activity in 4 of the 32 cases in the lipase series. Eight of the 29 cases of the amylase series had values less than 30 milligrams and the 7 with amylase values over 100 milligrams occurred in cases of chronic calculous cholecystitis.

OTHER DISEASES

Serum enzyme tests were done on 66 cases with diseases other than those already discussed. Elevated values were observed in 4 of the 37 cases in

the lipase group and in 7 of the 29 cases in the amylase group. The latter ranged between 100 and 200 milligrams. None of these cases came to operation or autopsy. However all but 2 had severe symptoms referable to the upper abdomen and 5 were shown by x-ray to have intra-abdominal neoplastic disease. We can only surmise that there was some pancreatic involvement in these cases, but because of lack of proof, no definite opinion as to the cause of these elevated enzyme values can be made. Helfitz, Probstern, and Gray have shown that renal insufficiency causes an increase in serum amylase and this factor probably explains some of the moderately elevated values. Only 1 patient presented an amylase value below 30 milligrams.

CORRELATION AND APPLICABILITY OF THE TWO ENZYME TESTS

Correlation between serum amylase and lipase activity was not as close as had been anticipated (Fig 2). The coefficient of correlation for the entire group was 0.66. Although this figure is statistically significant it may be concluded that of the factors governing the activity of these enzymes, only two-thirds are common to both and that an appreciable degree of independence exists. Calculation of regression of amylase on lipase failed to yield a significant regression coefficient, which is a further indication of an independent behavior of these enzymes.

Lipase was normal in the presence of elevated amylase more frequently (12 of 18 times) than amylase was normal in the presence of elevated lipase (4 of 10 times). However when tested by the Chi square method this difference was found to be nonsignificant.

Technically both serum amylase and lipase determinations can easily be performed by the ordinary hospital laboratory. However because

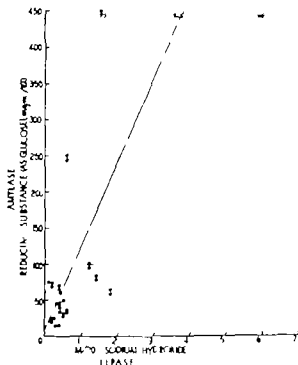


Fig 2. Relationship of serum between amylase and lipase.

TABLE IV—SERUM AMYLASE AND LIPASE IN OTHER DISEASE

Lipase						Amylase						
Total cases	c. N/50 NaOH					Total cases	Mgm glucose liberated/100 c.c.					
	-0.5	3-0.5	5-0	10-1.5	Over 5		Under 50	50-100	100-200	200-500	Over 500	
Per cent of total					Per cent of total							
27	30	6	7	6		30	1	5	4			

of the greater rapidity with which amylase can be measured (less than 1 hour) and the ease with which the ordinary blood sugar methods can be adapted to this test, amylase determinations are clinically more useful. This is especially true in cases of acute upper abdominal disease. The lipase determination as has been pointed out is helpful as an aid in the diagnosis of carcinoma of the head of the pancreas. In such cases speed is not necessary. Our experience also suggests the desirability of doing both tests in obscure cases.

EVALUATION OF STUDY

Evidence presented in this paper and in many others shows that the blood serum amylase and lipase are valuable aids in the diagnosis of acute pancreatitis provided the determinations are done soon after the onset of symptoms. It is also evident that alterations in the activity of these serum enzymes may be used to advantage in diagnosing carcinoma of the head of the pancreas. In this disease, the presence of painless jaundice, normal serum amylase and elevated serum lipase is a combination of diagnostic import.

Somogyi (16) states that low serum amylase is found only in cases in which some form or other of liver damage and subsequent impairment of liver function is present and Gray, Probst and Helfitz are in agreement with this view. In our study the group of cases with liver disease had more low serum amylase values and fewer high enzyme values than did any other group. However the low values did not occur with a sufficient degree of consistency to warrant the use of serum amylase determinations as a liver function test. Low amylase activity was somewhat more prevalent in cases of chronic jaundice (Table II) than in cases of acute jaundice.

In 1933 Foged pointed out that urine amylase was often elevated in cases of cholelithiasis with common duct stone, and in 1938, Branch and Zollinger in this country found high blood serum amylase in 3 of 6 cases. Millbourne has presented a group of 74 cases with obstructive jaundice due to stone in the common duct of which 53 per cent

had high values. It is interesting to note that 11 of these patients were proved to have had an accompanying acute pancreatitis. In our study all of the cases with common duct stone that had high values, in which the pancreas was examined, showed pathological changes in that organ and all those with normal values had normal pancreases. Although pancreatic exploration was not carried out in all of our cases, it would seem likely from these observations that elevated serum enzyme values in cases of calculous common duct obstruction were due to underlying pancreatic pathology. Therefore increased enzyme activity is not a test for stone in the common duct *per se*.

SUMMARY

1 The relative diagnostic value of serum amylase and serum lipase in patients with diseases of the pancreas, liver and gall bladder has been compared.

2 The normal values of serum amylase depend upon the blood sugar method employed in the measurement of reducing substances liberated by amylase action. When the Folin copper reduction method is used in the Somogyi technique, normal serum amylase averages 62 milligrams and ranges from 30 to 100 milligrams.

3 Both amylase and lipase determinations are of great value as aids in diagnosing acute pancreatitis.

4 In carcinoma of the head of the pancreas, the serum lipase is usually increased and the serum amylase normal.

5 In liver disease the serum amylase activity is likely to be depressed but not with sufficient consistency to enable the use of this change in diagnosis.

6 The serum enzyme activity in cases of calculous common duct obstruction appears to be increased only in those cases in which the pancreas has been damaged.

7 The coefficient of correlation between serum amylase and lipase activity was 0.66. The value of amylase and lipase determinations thus is increased when both enzymes are determined.

8. Both enzyme tests can easily be done by the ordinary hospital laboratory. The serum amylase test is usually the most useful clinically because of the rapidity with which it can be performed.

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THE MISSION OF SURGICAL SPECIALISTS IN THE U S ARMY

IN February 1942 the Surgeon General established in his office Professional Consultant Divisions in Surgery Medicine and Neuropsychiatry thereby giving official cognizance to the importance of these specialized clinical functions and setting the standard of organization of professional services in other echelons of the Medical Department of the Army Subsequently and as rapidly as the needs dictated each of these professional consultant divisions expanded its staff and organization to include functional representation in their respective fields of specialized endeavor Thus in the surgical consultants division there have been created branches in general surgery orthopedic surgery neurosurgery ophthalmology otolaryngology radiation transfusion therapy and chemical warfare The functions of these professional consultant divisions may be broadly described as administrative correlative advisory educational and analytical

In addition to the Chief Surgical Consultant and his staff in the Office of The Surgeon General Surgical Consultants have been assigned to every Service Command in the Zone of Interior to all active Theaters of Operation and to every active army Selected on the basis of their special training and background and their eminent qualifications in their respective fields of endeavor these consultants are concerned essentially with the maintenance of the highest standards of medical practice It is their function to evaluate promote and improve further the quality of medical care by every possible means to interpret the professional policies of the Surgeon General and to aid in their implementation The proper performance of these functions necessarily involves an appraisal of all factors concerned with the professional services in medical installations the quality numbers distribution and assignment of professional personnel the diagnostic facilities, the availability and suitability of equipment and supplies for professional needs and other auxiliary services which are essential to the welfare and morale of patients The surgical consultants exercise their functions by assisting and advising the Service Command and Theater Surgeons on all matters pertaining to surgical practice including particularly the organization and program of surgical services in medical installations and the quality distribution and proper assignments of professional personnel by providing advice on newer developments in diagnosis and treatment by stimulating interest in professional problems and aiding in their investigation and by encouraging educational programs such as conferences ward rounds and journal clubs The

excellent manner in which they have executed their functions the industry and zeal they have manifested and the high standards of medical practice in the Army they have helped to elevate are most gratifying. That this entire program was inaugurated with wisdom and foresight is demonstrated by the fact that from surgical consultants in overseas theaters as well as service commands have been received valuable reports which have made possible appropriate modifications of existing medicomilitary practice and the institution of more efficacious procedures and innovations.

In the overseas theaters of operation the surgical consultants have shouldered their great responsibilities in a most commendable manner. By assiduous and unrelenting attention to the multitudinous personnel and professional problems which have arisen they have been responsible in no small measure for the effective surgical treatment which has saved more lives in this war than in any previous conflict in the history of the world. Constant vigilance for methods of implementing earlier and better surgery with a determined effort toward reducing even further an already unprecedentedly low mortality among the wounded has characterized their activities from the date of their assignment.

Civilian surgical consultants in the United States have likewise been appointed on the recommendations of the Surgical Consultants Division of the Office of the Surgeon General. In the specialized surgical fields civilian consultants have been appointed in ophthalmology otolaryngology neurosurgery orthopedic surgery surgery of the hand thoracic surgery and anesthesia. These civilian consultants who have given of their time so unstintingly whenever called upon have periodically visited hospital installations in the Service Commands and have furnished to the Surgeon General reports which include con-

structive criticism with suggestions for further elevating the caliber of surgical care being rendered in the Army. The favorable comments which these civilian consultants chosen for their eminence in their particular specialties, have made in regard to the high level of surgical practice observed have been a source of pride to the Surgeon General.

The creation of specialized surgical centers in the general hospitals in the Zone of Interior represents another progressive innovation in the Medical Department's program of furthering professional service and clearly reflects the Surgeon General's policy to foster specialized surgical care by highly trained specialists. At the present time in the field of surgery there have been established 48 units in general hospitals in the Zone of the Interior designated for the specialized care of the various types of injuries and surgical diseases. These include 6 centers for amputations 21 for neurosurgery 5 for thoracic surgery 3 for vascular surgery 8 for plastic surgery 8 for ophthalmologic surgery and 2 for the rehabilitation of the blind and 3 for the deaf. The centers have been staffed by well trained and highly qualified specialists in these various surgical fields of endeavor and no effort has been spared in providing them with the most modern technical equipment and specialized facilities required for this type of work. It should be said that these installations afford an ample opportunity for on the job training to young surgeons whose apprenticeship was interrupted by the war. Obviously nothing approximating the complete training in residency afforded by civilian teaching hospitals in peace time can be accomplished for many reasons. However it is not too much to say that this training in these designated hospitals under civilian surgical specialists, teachers in uniform compares favorably in caliber with its counterpart in civil practice and, in

all likelihood all of the specialty boards will grant for it certain credit in their requirements for certification. Indeed the American Board of Surgery has already agreed to give 1 year's credit for training in army hospitals.

Recognizing the importance of specialized training and the significance of its efficient utilization the Surgical Consultants Division in the Office of the Surgeon General has since its inception been intensely interested in the proper assignment of surgical personnel and has continued to devote considerable effort in this direction. It has been considered essential to assure the assignment of suitably qualified personnel to key surgical positions in army hospitals. From time to time there has appeared some criticism of malassignments in consonant rank and other evidence of round pegs in square holes. In an organization which has mushroomed in growth from less than 1300 members to nearly 35 times this number it is only reasonable to expect such administrative errors particularly during the rapid expansion. However the correction of these unfortunate but sincere mistakes has been vigorously pursued and a determined effort has been made to reduce them to a minimum. That this effort has been attended by some measure of success is demonstrated by the results of a recent survey of surgical personnel in the Army.

The accompanying table is an analysis of assignments of surgeons who are certified by specialty boards or have equivalent qualifications and are now serving in army installations in the Zone of the Interior.

This sample of 922 qualified and certificated surgical specialists shows that 96 per cent of the surgeons in these categories recognized by the Army are doing surgery in their own specialty in army hospitals. The 37 surgeons in the same category who are not doing surgery are serving as consulting surgeons either in the

	Non-surgical duties		Surgical duties		Total
	N	Per cent	N	Per cent	
General surgery	3	9.9	90	90	33
Neurosurgery			37	100	7
Orthopedic surgery	7	4.6	143	93.4	50
Urological surgery			86	100	86
Plastic surgery			4	100	14
Thoracic surgery			8	100	8
Ophthalmology	3	8	67	95	70
Otolaryngology	4		96	95	100
ZENT			15	100	35
Total	37	4	835	96	922

Office of the Surgeon General or in the nine Service Commands into which the Continental United States is divided. That a parallel disposition of talent be carried out in the theaters of operation has been a goal toward which the Army has pointed. The very fact that so many hospital units were sponsored by medical schools, clinics and teaching hospitals enabled the Army at the beginning of the war to concentrate a large pool of surgical talent which, being accepted for overseas service, guaranteed a distribution of surgical specialists in the theaters of operation. These specialists distributed throughout the theater to other installations less fortunately manned elevated the general level of surgical service insuring to the wounded man skilled care.

The program of supervision, co-ordination and policy-making originated in the Surgeon General's Office and integrated throughout the various echelons in the Zone of the Interior and the theaters of operations has resulted in an equitable distribution of surgical talent and a consequent maintenance of a high standard of surgery always comparable frequently superior to that available to a cross section of the population of the country.

Indeed the ambition of the Surgical Consultants to the Surgeon General of the U S

Army has been to establish definitive treatment of wounded soldiers in a parallel direction to the trend in specialization which has been fostered in this country during the last two decades. Medical schools have emphasized the importance of formalizing programs of apprenticeship in the various special fields of surgical endeavor and the Army by reason of having the vast majority of the young vigorous well trained surgical specialists in its ranks has profited thereby. As a result of this educational development more capable young surgeons were available to the Army at beginning of this war than was the case in any army hitherto mobilized anywhere in any war. It but remained for the Surgeon General's Office to implement their assignment in appropriate installations to the end that their talents might be used to the fullest. The test of this endeavor is reflected in present day mortality and morbidity statistics.

That the Army of the future may profit by this experience to the end that it develops specialization within its own ranks and encourages formalized training by its own officers for its own officers in large army hospital clinic centers geographically distributed through the country is a dream not impossible of realization. There are in the Army at this time a sufficient number of civilian surgeons who could and would willingly forward such a program were they encouraged in the belief that their suggestions and examples would be welcome and appreciated. Planning to this end is imperative. The responsibilities of the surgical profession in an expanding internationalism challenge the imagination.

Where there is no vision the people perish

Proverbs XXIX 18

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PERIPHERAL NERVE SURGERY

IT is agreed by neurological surgeons and neurologists that the principles which underlie the surgical treatment of peripheral nerve injuries are not well understood by the civilian and military surgeons who are in positions to give these patients the most advantageous early and primary care.

The ideal surgical method of repairing a peripheral nerve injury is an accurate end-to-end apposition of the divided ends at the earliest possible moment following division with the finest possible suture material which passes through the epineurium of the nerve trunk.

Peripheral nerves undergo degeneration through their entire course distal to the site of injury. Degeneration extends to the nerve endings on the muscle fibers. The denervated muscles atrophy, fibrosis occurs in unused joints, tendons lengthen or shorten in brief the entire effector mechanism which makes an extremity useful is affected. Muscle atrophy and contractures cannot be prevented by physical therapy methods alone. Regeneration of the nerve endings in the muscle must occur before muscle fibers have been completely destroyed. It is of little use to obtain an excellent anatomical union of a fractured bone if the paralyzed and atrophied muscles prevent the movement of the extremity.

An end-to-end apposition of a divided nerve end should never be deliberately postponed. The circumstances surrounding the peripheral nerve injuries of warfare may often necessitate a delay in repair but the fear of an infection in the wound should not be used as a reason to delay the apposition of nerve ends. It has been shown that nerve regeneration may take place in an infected wound and only when the nerve fascicles within the nerve trunk are involved does infection interfere with the

downgrowth of nerve fibers. Even under the most adverse circumstances the apposition of divided nerve ends will prevent their retraction and the growth of large neuromas which later will necessitate the bridging of a large continuity defect.

It has also been shown that if in the opinion of the surgeon the sulfonamide drugs should be used locally or systemically in an effort to control suppuration in the wound they will not interfere with the regeneration of nerve fibers. There is clinical experience in war injuries to show that infected wounds which have healed may be opened, the nerve sutured and closed after the introduction of the sulfonamides with little or no danger of activating latent bacteria. This experience contraindicates the long intervals that have been respected in the past before it was deemed safe to reopen the wound and suture a divided nerve. All of these factors must be weighed carefully to insure the earliest possible apposition of a divided peripheral nerve.

If there has been a destruction of nerve tissue which makes end to-end apposition difficult every surgical procedure such as transposition of the nerve trunk from its normal anatomical bed to a shorter course and the flexion or extension of adjacent joints, should be employed to obtain an end to-end approximation.

If the defect in substance is too great to be bridged by these methods then there is enough experimental and encouraging clinical evidence to justify the use of fresh autogenous or homogenous nerve grafts of approximately the same size as the divided nerve. Occasionally it is justifiable to sacrifice one nerve in an extremity to provide a graft for another provided both are severely injured. Such an autogenous graft may provide useful function to an otherwise useless extremity. More often, however homogenous grafts must be em-

ployed as a more practical method of bridging a large defect.

Grafts act as a pathway for the regenerating nerve fibers from the central segment of the divided nerve. Although the ectodermal tissue such as nerve fibers, myelin sheaths, and Schwann (neurilemma) cells undergoes necrosis most of the mesodermal tissue remains alive. This is most marked in the periphery of the graft where the blood supply is restored soon after transplantation. Capillaries grow from the periphery into the center of the graft and the phagocytes ingest the necrotic material. Soon the endoneural and perineural mesodermal elements proliferate throughout the graft and join with the proliferated mesodermal elements of the central and distal nerve segments at the suture line. The regenerating nerve fibers follow the path of the mesodermal fibers through the suture lines and the graft. Therefore the proliferation of the mesodermal cells and the formation of mesodermal collagenous fibers are of the utmost importance for the regeneration of a nerve through a graft. Until recently most investigators have underestimated the importance of this mesodermal proliferation in the process of nerve regeneration, because they failed to visualize the mesodermal tissue in their nerve fiber stains and to see its relation to the regenerating Schwann cells and nerve fibers.

The survival of the mesodermal elements is important in the transplanted grafts and therefore it is necessary for the graft to be fresh if it is to be successful. Stored grafts which have been fixed in formalin and dehydrated in alcohol are bound to be unsuccessful because they are dead and remain dead. When transplanted these fixed grafts undergo complete necrosis and it requires a long time for capillaries to proliferate from the surrounding tissues, penetrate the graft, and for the necrotic material to be removed. Delaying the

blood supply even to a fresh graft by surrounding the suture lines or the entire graft with metallic sheaths or tubes of any kind will only enhance the necrosis and keep the mesodermal tissue from proliferating. The small adhesions which form about the suture lines and the transplanted graft carry blood vessels which supply the graft. Necrosis of the graft results in a complete disturbance of its structure and is the most serious factor which will prevent the return of a large number of regenerating nerve fibers to their appropriate end organs.

Evaluation of the results of peripheral nerve end-to-end sutures and the use of nerve grafts during World War I has been unsuccessful for many reasons, the most important of which has been the lack of uniformity in the examination of recovery of motor and sensory function and in the criteria to establish such recovery and second the lack of follow up records of the patients. At present there is a tendency to evaluate the results of grafts after periods of time far too short following opera-

tion. Six months or more frequently elapses following an end-to-end suture under ideal conditions before the first evidence of recovery occurs, and to expect evidence of recovery after the same period of time following the use of a homogenous graft is expecting the impossible.

The Surgeon General has already taken steps to insure the examination of patients with peripheral nerve injuries postoperatively while they remain within the Army. It is to be hoped that the Veterans Administration will make a contribution to the progress of surgery by making it incumbent upon the discharged veteran to have a periodical examination by competent neurologists and neurological surgeons until the full data upon the progress of his recovery have been obtained. This dependency of compensation upon periodical examinations is one of the outstanding and most important features of the British plan for the care of disabled soldiers who have suffered peripheral nerve injuries.

LOYAL DAVIS

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

PREPARED by Simmons and his assistants in the Medical Intelligence Division of the Preventive Medicine Service in the Office of the Surgeon General of the United States Army *Global Epidemiology* represents an excursion into the unexplored field of geo-medicine bringing together in one place certain data on medical, health and sanitary conditions of various geographic areas of the world. — This first volume includes medical information about India the Far East and the Pacific area. The index presents 34 main divisions but information from 190 separate areas is included. It is a compilation of facts of medical interest contributed from many sources the first objective of which was to provide material for the intelligent planning for medical care of troops. What remains after the deletion of material of military value is presented in this first volume.

This considerable collection of medical information from 34 countries and island groups has been

presented as follows (1) geography and climate (2) public health (3) medical facilities (4) diseases (5) summary. Each of the above divisions contains what is known of medical interest in each locality. Sketch maps of the localities under consideration and an appendix containing maps prepared by the Preventive Medicine Division showing the distribution of 14 important diseases throughout the world illustrate the epidemiological features. A striking fact, repeatedly brought out in this book, is that through all possible variations of geography and climate and among several ethnological groups in the areas discussed the public health services and the medical facilities fall far short of the need in that most of the diseases prevalent in those areas are those which could effectively be dealt with by adequate administration and facilities. The incidence of illness and death due to dangerous animals in the tropics is very low comparatively.

This first volume is a valuable contribution to the understanding of the medical problems of the areas under consideration. The information offered is dependable and will be extremely useful to persons responsible for health and hygiene in these areas.

HENRY R. JACOBS.

GLOBAL EPIDEMIOLOGY: A GEOGRAPHY OF DISEASE AND SANITATION. By JAMES S. SIMMONS, B.S., M.D. PH.D. Dr.P.H., Sc.D. (Hon.). Tom F. Whayne, A.B., M.D. Gaylord West Anderson, A.B. M.D. Dr.P.H. Harold M. Horack, B.S. M.D. and collaborators. Vol. Philadelphia, London, Montreal J. B. Lippincott Co. 1944.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

TRANSACTIONS OF THE SIXTY-FIFTH MEETING OF THE AMERICAN SURGICAL ASSOCIATION HELD AT THE TROVINO HALL, NORTHWESTERN UNIVERSITY, CHICAGO, ILL. MAY 3-7, 1944. Edited by Walter Estell Lee, M.D. Vol. 65. Philadelphia J. B. Lippincott Co. 1944.

SURGERY OF MODERN WARFARE. Edited by Hamilton Bailey, F.R.C.S., and C. Allan Birch, M.D. M.R.C.P., D.C.H., D.P.H., M.M.S.A. Vols. 1 and 2. 3d ed. Baltimore The Williams & Wilkins Co. 1944.

ARTERIAL INJURIES: EARLY DIAGNOSIS AND TREATMENT By the Vascular Injuries Sub-Committee of the M.R.C. War Wounds Committee. Medical Research Council War Memo. No. 13. London H. M. Stationery Office, 1944.

SEVERE LETHARGY. By H. F. Moseley, M.A. D.M. M.Ch.(Oxon.) F.R.C.S. (Eng. and C.) F.A.C.S. Springfield, Ill. Charles C. Thomas, 1945.

THE 1944 YEAR BOOK OF INDUSTRIAL AND ORTHOPEDIC SURGERY. Edited by Charles F. Painter M.D. Chicago The Year Book Publishers, Inc. 1945.

SPINA BIFIDA AND CRANIUM BIFIDUM. Papers reprinted from the *New England Journal of Medicine* with the addition of a comprehensive bibliography. By Francis D. Ingraham M.D. et al. The Children's Hospital, Boston. Cambridge, Mass.: Harvard University Press, 1943, 1944.

MODERN METHODS OF AMPUTATION. By Edmondo Vasconcelos. With an Introductory Survey of The Development of Amputation by Major Gen. Norman T. Kirk, M.C. New York The Philosophical Library 1945.

A TEXTBOOK OF PATHOLOGY OF LABOR, THE PUERPERIUM AND THE NEWBORN. By Charles O. McCormick, A.B. M.D. F.A.C.S. St. Louis The C. V. Mosby Co., 1944.

THE ABORTION PROBLEM. Proceedings of the Conference Held under the Auspices of the National Committee on Maternal Health, Inc., at the New York Academy of Medicine, June 19th and 20th, 1942. Howard C. Taylor Jr., M.D., Conference Chairman. Baltimore The Williams & Wilkins Co. 1944.

PYE'S SURGICAL HANDBOOK: A MANUAL OF SURGICAL MANIPULATIONS, MINOR SURGERY AND OTHER MATTERS CONNECTED WITH THE WORK OF SURGICAL DRESSERS, HOUSE SURGEONS, AND PRACTITIONERS. Edited by Hamilton Bailey F.R.C.S. Eng. 14th ed. Baltimore The Williams & Wilkins Co. 1944.

CORRESPONDENCE

MEDICAL CORPS, UNITED STATES ARMY

To the Editor: Ever since reading Dr Lawrence Kubie's editorial in the January issue of *SURGERY, GYNECOLOGY AND OBSTETRICS* I have intended to write you.

Dr Kubie is a man of keen intellect, and I know that his interest in the matter of specialization in the armed services is a sincere one. He wants to help and we want him to help. His criticisms are, in some instances just but in others I think, they are unjust.

We have always had a number of men in the various specialties who were good professionally but who never tried to qualify before the various Boards. No doubt they should be given more encouragement. Again, we have always had many stations where we had to keep good all-round qualified men as they were more or less on their own. These men never had a chance to qualify in any specialty. The Army does not try to make every man a general practitioner however. We know that in time of peace we are preparing for war and every Regular Army officer must in time of war drop his professional work and take up the burden of military medical administration in some form.

There is always a small group of medical officers who are specialists in medical field work. These men are the ones we have to depend on in time of war to go out in key positions with the field forces. They go through our various service schools and are trained for this particular type of duty.

I do not agree with Dr Kubie in his statement that there was a two year period of fumbling and uncertainty at the beginning of this war. We had a

very small reserve of trained specialists and I think the records show they were used to the greatest advantage. At first, there were many jobs to which specialists were assigned because there were not hands enough to do the work. In so far as the records of specialists are concerned, this office has never been reorganized but still follows the plan put into effect at the beginning of the war.

I agree with Dr Kubie that, following this war there should be much closer liaison between the Medical Corps and the various specialty boards and the special societies.

I do not agree with Dr Kubie that the services attract only the mediocre young physicians. I do not have the time nor the clerical help to make an exhaustive study of this, but I have selected one class at random and examined the records of all members. Most of these records contain signed statements from the deans of medical schools. The results in this class of 36 men were as follows: upper third, 13; middle third, 14; lower third, 3; no report, 4; very satisfactory, 1; good, 1—a total of 36. One man classed in the middle third was not so rated by his dean who simply gave him a general average of 85 per cent for the four years. Looking over the names in this class I note that many of the men in the middle third have superior war records.

This has been a much longer letter than I intended to write but I have stated my case and hope that you will bear with me.

With warmest personal regards, I am

Sincerely yours,

GEORGE F. LULL,
Major General, USA,
Deputy Surgeon General

February 1945

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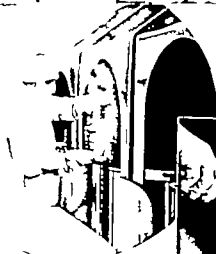
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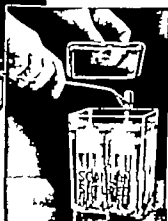
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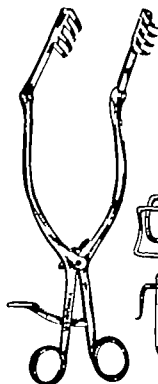
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GYNECOLOGY AND OBSTETRICS

An International Magazine, Published Monthly

VOLUME 80

MAY, 1945

NUMBER 5

THE NUTRITION OF PATIENTS WITH THERMAL BURNS

*
STANLEY M. LEVENSON M.D., CHARLES S. DAVIDSON M.D. C.M.
CHARLES C. LUND M.D., F.A.C.S., and F. H. L. TAYLOR Ph.D. Boston Massachusetts

LOSS of weight often marked has long been recognized as a serious complication in severely burned patients. However only in recent years has the problem of maintaining the nutrition of these patients been clearly recognized. With the increased use of plasma and the re-emphasis of the proper use of electrolyte solutions, many of the severely burned patients who formerly died of circulatory collapse are being brought through the early shock phase into the later period frequently characterized by marked nutritional disturbances. Thus the problem of malnutrition following thermal injury which was hitherto seen only occasionally must now be faced in an increasing number of patients.

The excess loss of nitrogenous products in the urine (9, 28, 42) and from the burned surfaces (24) together with the progressive reduction in plasma protein concentration (39, 42) indicate that actual body protein is depleted in these patients. Attempts to combat the weight loss by high caloric, high vitamin

and high protein diets have frequently been made in such patients (1), but there are few detailed studies of the actual nutritional requirements (14, 24, 43). The most recent report is that of CoTui (15) on 3 patients with third degree burns of varying severity. The present communication is concerned with a group of 32 individuals studied in the period November 1942 to August 1943, in each of whom an effort was made to determine and in some cases to meet the protein and caloric requirements and to ascertain to what extent factors such as age, nutritional status on entry and extent of third degree burn influenced the food requirement. In addition the problem of late liver damage is discussed.

METHODS

The food intake in terms of calories, protein, carbohydrate and fat was determined from records of the food ingested by the patients using standard tables (7). In several patients whose protein and caloric intake changed very little during certain periods of their course these figures were averaged. This was done in preparing the data for Chart 1 (after the second week), Chart 3 (after the twelfth week) and Chart 4 (after the eighth week). It was considered more representative of the facts to present the data in this way since the week to week variations were less than the errors inherent in the calculations.

From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard) and the Burn Assignment of the Surgical Services, Boston City Hospital, and the Departments of Medicine and Surgery, Harvard Medical School.

The work described in this paper was done in part under contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

The expenses of this investigation were defrayed in part by grant given "in recognition of Dr. Francis W. Peabody's services to the Foundation" by the Ella Sachs Peutz Foundation.

TABLE II.—CLASS I. PATIENTS WITH MODERATE BURNS

No. Age Sex	Per cent body surface burned Total of degrees	Chronic dis- ease	Complications				Diet				Nitrogen excretion		Plasma protein concentration gm./100 ml.	Dis- charge day	Result
			Fever	Local excrudi- tion	As- sida	Liver disease	Time (weeks)	Average calories	Daily food intake		Time (weeks)	Average daily urinary nitrogen (grams)			
									Protein (grams)	Nitrogen (grams)					
22 M	6							1400	70			7	Total + A. G. Normal throughout	13 ⁰⁰	Lived
								1700	140	22		14			
							3+	1700	120	20	3	17			
26 M	6							1400	70				Total + A. G. Normal throughout	17 ⁰⁰	Lived
								1600	80	2		10			
							3+	1700	90		3				
3 M	6							1400	70				Total + A. G. Normal throughout	20 ⁰⁰	Lived
								1900	30	19					
							3+	3000	30	21	3	7			
11 M	6							1400	70	11		6	Total + A. G. Normal throughout	17 ⁰⁰	Lived
								1900	15	20		3			
							3+	3000	15	22	3				
15 ^a M	6		1 ^b					200	60	9.6		14	Total + A. G. Normal throughout	64 ⁰⁰	Lived
								200	60	9.6		10			
							3+	2700	100		3+	9			
6 M	6							1400	70			16	Total + A. G. Normal throughout	20 ⁰⁰	Lived
								1700	30	21					
							3+	1900	140	22	3+				
7 M	6		3 ^c					400	70	17		14	Total normal throughout A. & G. 3. (Drug fever during 2d week; normal thereafter)	21 ⁰⁰	Lived
								1900	00	2.6		20			
							+	3000	30	24	3+	14			
8 M	8							1800	120			11	Total + A. G. Normal throughout	64 ⁰⁰	Lived
								1900	140	22					
							3+	1900	140	22	3	8			
											4	9			
67 ^d F	5 3				+			2000	90	14		9	See Chart	20 ⁰⁰	Lived
								2000	80	19		7			
							3+	1700	2	20	3	7			
												7			
20 30 F	2 3				+			1400	70				Total + A. G. Normal throughout	13 ⁰⁰	Lived
								1700	30	19		10			
							3+	300	1.17	20					
												7			
12 M	8							400	70			15	Total normal throughout A. & G. 3 during 1st week. Normal thereafter	28 ⁰⁰	Lived
								1900	148	24		16			
							3+	2600	140	23	3	9			
											4	13			

^aNutritional status on admission—good.^bNutritional status on admission—fair.^cNutritional status on admission—poor.^dNutritional status on discharge—good.^eNutritional status on discharge—fair.^fNutritional status on discharge—poor.

{Fever: a, Absent; 1, temperature up to 102 degrees for less than 1 week; 2, temperature up to 103 degrees for more than 1 week; 3, temperature up to 104 degrees for more than 1 week; 4, temperature greater than 104 degrees for over 1 week.

^bFever from noninfectious treatment.

{Local excretion: () slight, (s) moderate, (3) severe, (4) very severe.

TABLE II.—CLASS I PATIENTS WITH MODERATE BURNS—Continued

No.	Age Sex	Per cent body surface burned Total 3d degree	Chrom- body surface burned Total 3d degree	Complications				Diet				Nitrogen excretion		Plasma protein concentration gm / 100 ml	Dis- charge day	Result
				Fever	Local infection	Asse- mia	Liver disease	Time (weeks)	Average calories	Daily food intake		Time (weeks)	Average daily urinary nitrogen (grams)			
										Protein (grams)	Nitrogen (grams)					
20	M	6							1400	78				Total normal throughout. 1st week A 2-7, G 3. Normal thereafter	35	Lived
									300	5	20					
								3+	1700	140	12	3	7			
3	F	5				+		1	400	70			8	Total normal throughout. 4th week A 5, G 9. Normal throughout	87	Lived
									300	20	9		9			
								3+	3000	130		3				
												4	8			
4	F	3	3			+			1400	70				Total + A, G Normal throughout	55	Lived
									300		8					
								3+	3000	5	80	3				
5	F	20	7			+			1400	70			11	Total normal throughout. A fell to 2.4, G rose to 3. In 2d week and to 4 by the 6th week. By 3d week A up to 2.5, G down to 3.5	97††	Lived
									3000	80	6		10			
								3+	3000	70	9	3	7			
10†	M	6	+	2 ⁴					3000	90	4		6	Total + A, G. Normal throughout	8	Lived
									4000	60	10					
								3+	4500	160	15	3	1			
												4	1-5			
12	M	2	+	3					700	60	9.6		—	Total + A, G. Normal throughout	65**	Lived
									700	60	9.6		—			
								3+	3700	90	2.4	3	—			
15	F	8				+			700	90	4.4			Total + A, G. Normal until 4th week; total then fell to 4.4. A 5, G.	3 11	Died
									700	90	4.4					
								3+	700	90	1.4	2				

†Nutritional status on admission—good.

††Nutritional status on admission—fair.

‡Nutritional status on admission—poor.

§Nutritional status on discharge—good.

||Nutritional status on discharge—fair.

|||Nutritional status on discharge—poor.

†Fever: 1, temperature up to 38 degrees for less than 1 week; 2, temperature up to 39 degrees for more than 1 week but less than 2 weeks; 3, temperature up to 40 degrees for 2 weeks; 4, temperature greater than 40 degrees for over 2 weeks.

Fever from unknown cause.

§Local infection: () slight, (1) moderate, (2) severe, (3) very severe.

hypoalbuminemia and hyperglobulinemia with normal total plasma protein concentrations.

The *apparent* nitrogen balance was determined by comparing the total nitrogen intake from all sources with the nitrogen excretion. Nitrogen excretion was calculated by adding to the measured urinary excretion 10 per cent of the nitrogen intake to account for stool nitrogen. Loss of nitrogenous substances from the burn surface was not measured and thus could not be used in calculating nitrogen balance. For this reason, nitrogen balance is re-

ferred to as *apparent* rather than *true* nitrogen balance.

The *apparent* nitrogen balances of the 14 patients in this group for whom there was adequate data show that, during the first week, 6 were in *apparent* mild negative balance (10 to 50 gm per day) while 8 were in *apparent* positive balance (10 to 120 gm per day). By the 2d week, 12 had an *apparent* positive balance (10 to 140 gm daily) while 2 had an *apparent* negative balance of about 20 grams daily. During the 3d week, only 12 of the 14 were followed. All were in *apparent*

TABLE III.—CLASS II. PATIENTS WITH SEVERE BURNS

No.	Age	Sex	Per cent body surface burned (Total) 3d degree	Chronic alcoholic habit	Complications				Diet				Nitrogen excretion		Plasma protein concentration gm./100 ml.	Discharge day	Result	
					Fever	Local excruciation	Anaemia	Liver disease	Time (weeks)	Average calories	Daily food intake		Time (weeks)	Average daily urinary nitrogen (grams)				
											Protein (grams)	Nitrogen (grams)						
8	20	M	5		3	3	+	+		1,800	70			10		See Chart 5	120 th	Lived
										1,800	120	18		6				
									2-10	700	25	20	3					
									30+	1,700	58	24						
20	17	F	10		1		+			900	60			—		Remained normal with slight rise in globulin and fall in albumin	35 th	Lived
										2,000	30	10		8.5				
									3+	4,500	180	20	3	8.5				
													4	8.5				
21	20	F	10							1,400	70					Remained above 4 and with A + G normal	120 th	Lived
										2,200	30							
									3+	3,000	130		3					
22	20	F	1		3		+			1,400	70	11				Normal to 5th week falling to 3.6 at 8th week (A 3.0, G 3.7) rose to normal by 10th week	100 th	Lived
										3,000	25	20						
									3+	3,000	40							
17	20	F	3		3		+			1,400	70					Remained above 5	70 th	Lived
										3,000	100	6						
									3+	3,000	30	10						
24	23	M	20			3	+			1,800	70	14				Total fell to 4.8 during 1st week A 3.0, G 3.0. Then rose to 5.8 by 6th week (A 3.0, G 3.6)	40 th	Died
										1,900	300	32						
									3+	3,000	300+	45	3	16				
													Sub					
5 th	20	M	20		3		+			900	60	9.6		5		Normal in 1st 3 weeks. No further data	10 th	Died (at another hospital)
										3,000	100	16		20				
									3	3,000	5	20		11.5				
26	20	F	20			3	+			1,800	60	9.6		14		See Chart	37 th	Died
										300	80	1.3		3.5				
									3+	3,000	100	16	2	6				
27	23	M	45				+			1,800	60	9.6		30		See Chart 3	30 th	Lived
										2-3	1,100	40	14		10			
										4-7	3,000	300	16	3	13			
										8-11	2,500	30	20.8	Sub	12			
									1-26	3,000	260	45						
28 th	2	M	20						+	300	300	20				Total remained normal with gradual fall in A to 4 and rise in G to 7	10 th	Died
									3									

*Nutritional status on admission—good.

†Nutritional status on admission—fair.

‡Nutritional status on admission—poor.

§Nutritional status on discharge—good.

||Nutritional status on discharge—fair.

¶Nutritional status on discharge—poor.

[Fever: 0, Absent; 1, temperature up to 100 degrees for less than 1 week; 2, temperature up to 102 degrees for more than 1 week but less than 2 weeks; 3, temperature up to 103 degrees for 2 weeks; 4, temperature greater than 104 degrees for over 2 weeks.]

[Local condition: (1) slight, (2) moderate, (3) severe, (4) very severe.]

TABLE III.—CLASS II. PATIENTS WITH SEVERE BURNS—Continued

No. Age Sex	Per cent body surface burned Total 3d degree	Chronic alcohol- ism	Complications				Diet				Nitrogen excretion		Plasma protein concentration gm /100 ml.	Dis- charge day	Result		
			Fever†	Local excretion‡	Ase- mia	Liver disease	Time (weeks)	Average calories	Daily food intake		Time (weeks)	Average daily urinary nitrogen (grams)					
									Protein (grams)	Nitrogen (grams)							
10 10 M	10 15	+	4	3	+	+		1800	60	0.6		14	See Chart 4	10††	Lived		
							1-6	800	60	4.4		3					
							7-8	1500	130	1.0	3						
							9-11	2000	100	3	Sub.	1-					
14 14 M	30 30	+		3	+	+		400	70	1			Varied between 4.3 and 1.7 with A. 1.0 and G. 2.6 to 3.6	8 ††	Died		
								500	5	0.0							
							3	3500	140								
15 15 M	33 45	+	3	4	+			300	60	0.6	1	14	Total remained normal with gradual rise in G. to 3.6 and fall of A. to	11††	Died		
								800	100	1.0		4					
							3	900	30	1.4	3	6					
							4	580	25	.3	Sub.	4					
16 16 F	65 85	+	3	4	+	+		300	60	1.4			Total gradually (all to 3.1 (A. 0.0 and G.)	17††	Died		
								1400	70	3							
							3	800	90	3							
							4	400	70								

*Nutritional status on admission—poor

†Nutritional status on admission—fair

‡Nutritional status on admission—poor

§Nutritional status on discharge—good

||Nutritional status on discharge—fair

††Nutritional status on discharge—poor

§Fever: 0, Afebrile; 1, temperature up to 101 degrees for less than 1 week; 2, temperature up to 102 degrees for more than 1 week; 3, temperature up to 103 degrees for more than 2 weeks; 4, temperature greater than 104 degrees for over 1 month.

||Local excretion () slight, () moderate (3) severe, (4) very severe

positive balance of from 10 to 120 grams per day. Healing of the second degree areas was uncomplicated. The granulations in the third degree areas appeared pink and healthy and grafts took satisfactorily. All the patients in this class of small burns in well nourished patients lived. Fourteen of the 15 maintained their weight and were in good nutritional status on discharge. The remaining patient (Case 15) who was the most severely burned in this group showed moderate loss of weight. The length of the hospital admissions was from 17 to 197 days.

There were 3 patients with moderate burns who were in poor nutritional status on entry. Two of these (Cases 16 and 17) suffered from chronic alcoholism in addition. Neither had evidence of cirrhosis. Their food intake averaged 150 to 160 grams of protein with 3500 to 4000 calories after the 1st and 2d weeks respectively. Until then their food intake had been 60 to 90 grams of protein and 1200 to 2000 calories daily. Daily urinary nitrogen

excretion was studied in patient 16 and was within normal limits. During the first week he was in apparent negative nitrogen balance and in the subsequent 2 weeks in apparent positive balance of about 12 grams of nitrogen per day. Neither patient developed hypoproteinemia. Both gained weight. The granulations of the third degree areas were firm and pink and grafting was completely successful. On discharge both were in much better nutritional status than upon admission.

The third patient (Case 18) was a senile woman of 75 years who on admission was almost cachectic. She had a poor appetite and would take almost nothing by mouth. Therefore she was fed by stomach tube a mixture of milk and sugar amounting to 90 grams of protein and 1700 calories per day. This was an insufficient food intake but when more food was given gastrointestinal disturbances, especially distention and diarrhea became distressing symptoms. However she did not appear to lose much weight and seemed to be

making reasonable progress toward recovery when she died after a very short illness, of bronchopneumonia.

Class II Severe burns In the group of 14 patients with severe burns, metabolic and nutritional disturbances were frequent and severe. The patients who were in *good nutritional status* on admission to the hospital will be considered first.

Food intake during the first week was low—60 to 90 grams of protein and 1,200 to 1,800 calories daily. Their appetites improved during the 2d week, and by the 3d week all but 3 (Cases 25, 26, and 27) were receiving from 140 to 300 grams of protein and 2,000 to 5,000 calories daily. Patient 25 was a boy of 19 years who was delirious. His appetite was not good and it was only with considerable coaxing that he ate a diet of 100 to 125 grams of protein and 2,000 to 3,000 calories. He was transferred at the end of 3 weeks to another hospital and died at the end of the 4th week. The diets of patients 26 and 27 are discussed in detail in the case report section. In short patient 26 was a girl, aged 22 years whose appetite was only fair. She refused supplementary feedings by tube or by vein. Her food intake was about 100 grams of protein and 2,000 calories daily. Patient 27, a male aged 22 years, took up to 100 grams of protein and 2,000 calories daily during the first 7 weeks, and then 130 grams of protein and 2,500 calories daily for the next 5 weeks. Thereafter his intake was raised to 300 grams of protein and 5,000 calories daily by means of gavage and intravenous supplements.

In contrast to the patients in Group I there was definite evidence of increased urinary nitrogen excretion in many of these patients with more severe burns. Thus, of 5 in whom such measurements were made 2 (Cases 24 and 27) excreted greater than 20 grams per day, 2 (Cases 19 and 25) between 15 and 20 grams, and 1 (Case 26) between 12 and 15 grams, while none excreted less than 12 grams daily during the 1st week. Thereafter the urinary nitrogen excretion fell so that during the 3d week of the 6 patients followed 4 (Cases 19, 20, 25, and 26) excreted less than 12 grams per day, while 2 (Cases 24 and 27) continued to excrete more than 15 grams per

day. After the 3d week the urinary nitrogen excretion was normal.

Considering the low food intake and excessive nitrogen excretion during the first weeks, it is not surprising to find that the *apparent* nitrogen balances in these patients were all negative in amounts from 4.0 grams to 21.0 grams per day during this time. However by the 3d week as the food intake was increased and the nitrogen excretion fell off 5 of the 6 patients were in *apparent* positive balance (8.0 gm to 18.0 gm per day) and only one (Case 27) was still in *apparent* negative balance (4.0 gm per day). Thereafter the 3 patients (Cases 20, 24, and 27) followed were in *apparent* positive nitrogen balance.

All patients in this group lost weight early in the course of their illness. However in the 5 patients with the less severe burns, the weight loss was moderate and was not progressive (see Figs. 12 to 17). In 3 (Cases 20, 21, and 23) the plasma protein concentration remained essentially normal. The other 2 showed significant plasma protein changes. Patient 22 had a normal plasma protein concentration until the 5th week when there began a gradual decline to a level of 3.6 grams per 100 milliliters by the 8th week. However the plasma proteins rose above 4.5 grams per 100 milliliters within the next week and were normal by the 20th week after injury. Patient 19 (whose course is detailed in the case report section) had a normal plasma protein concentration until the onset of jaundice in the 11th week. At this time the plasma albumin fell to 2.0 grams per 100 milliliters, while the globulin remained at a level of 2.3 grams per 100 milliliters. In the next 3 weeks with the regression of the jaundice there was a gradual return of the albumin fraction to normal.

These 5 patients lived. Although they were still somewhat under weight on discharge, their general nutritional status was good. The third degree areas had been grafted without difficulty, the granulations having been firm and healthy in appearance.

Patient 25 was followed for only 3 weeks. During this time his plasma proteins remained normal and weight loss was only moderate.

The remaining 3 patients in this group (Cases 24, 26, and 27) who had the most ex-

tensive third degree burns exhibited the most marked nutritional disturbances. The courses of 2 (Cases 26 and 27) are detailed in the case report section. In these 2 weight loss was extreme and there was a progressive fall in the plasma protein concentration. The granulations in the third degree areas were soggy, edematous and friable and there was considerably more exudate than from normal granulations. Patient 26 refused supplementary feedings, continued to lose weight and died of malnutrition and infection on the 157th day. In contrast patient 27 responded to a very high protein and caloric intake with a gain in weight and loss of edema so that skin grafting could be done. He was discharged on the 363d day. Patient 24 lost a moderate amount of weight in the first 2 weeks but thereafter on a diet of above 300 grams of protein and 3 000 calories daily weight was maintained. His plasma protein concentration fell to 4.8 grams per 100 milliliters during the first week but rose to 5.8 by the 6th week. The albumin concentration at this time was 2.3 and the globulin 3.6. Although sloughing of the dead tissue in the third degree areas was complete by the 4th week there was no granulation tissue. The patient appeared to be doing fairly well when he developed an acute fulminating pyelonephritis and died on the 46th day.

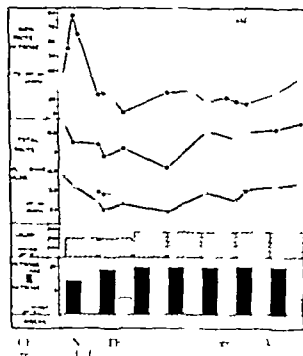
Since the patients in this group were in *apparent positive nitrogen balance* during most of their course and at the same time lost weight roughly in proportion to the extent of third degree burns it is clear that the surface loss of protein was important. As an example patient 27 was in *apparent* cumulative positive nitrogen balance of about 1.3 kilograms at the 18th week following the burn. His weight nevertheless was 55 pounds below his admission weight.

There were 5 patients with severe burns who were in inadequate nutritional status on entry. Patient 31, 50 years of age, a chronic alcoholic, had a 45 per cent third degree burn. His intake varied from 60 to 150 grams of protein daily and 1 200 to 2 500 calories. Urinary nitrogen excretion was 24.0 grams daily during the 1st week and 14.0 to 16.0 grams thereafter. He lost considerable weight, his plasma

albumin fell and the granulating third degree areas were soggy and friable. He died on the 33d hospital day, the precipitating cause being bronchopneumonia.

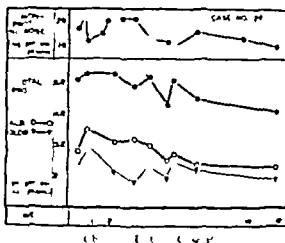
Patient 32, a woman of 32 years, also with chronic alcoholism, had third degree burns of 55 per cent of her body surface and had a course similar to that described for patient 31. Fever was high and prolonged. By the 7th day her hemoglobin had fallen to 45 per cent and thereafter frequent blood transfusions were required to keep her hemoglobin about 70 per cent. Her food intake was 60 to 90 grams of protein and 1 200 to 1 800 calories daily. Urinary nitrogen excretion was 14 to 15 grams daily for the first 2 weeks, 12 to 13 grams daily thereafter. She lost considerable weight, the plasma protein concentration fell slowly to 3.1 grams per 100 milliliters. There was marked exudation from the third degree areas, the granulations being soft and friable. During the 4th week she became slightly jaundiced and died on the 27th hospital day of bronchopneumonia.

Patient 30, a bartender, 34 years of age, also admitted to a considerable alcoholic intake. He was markedly overweight (350 pounds). He had third degree burns of 20 per cent of his body surface and an additional 10 per cent involved with second degree burns. His food intake during the 1st week was about 70 grams of protein and 1 400 calories daily but by the 3d week it had risen to 140 grams of protein and 3 500 calories daily at about which level it remained. Plasma protein concentration varied between 4.3 and 5.7 grams per 100 milliliters with the albumin fraction being between 1.7 and 2.1 grams and the globulin fraction 2.6 to 3.6 grams. His icteric index was normal throughout. Repeated blood transfusions were required to keep the hemoglobin at a satisfactory level. His temperature was about 101 degrees during most of his admission and there was moderate exudation from the third degree areas. There was no peripheral edema and the granulation tissue appeared firm. He appeared to be doing fairly well although it was clear that he had lost a considerable amount of weight until the 11th week when he suddenly developed bronchopneumonia and died. At autopsy a firm



tatively but with high creatinemia was treated and he had to be put on dialysis.

For the next six months the patient was hospitalized in the medical ward. He was treated with a diet of 100 grams protein and 400 calories daily. His creatinemia was very high and there was no gain in weight. His weight was 100 pounds and excretion from the third to the sixth week was light. There was no fall in hemoglobin concentration. His total plasma protein concentration remained at 6.5 grams per 100 milliliters but the albumin fraction fell to 2.4 grams while the globulin fraction rose to 4.1 grams. His weight was maintained. During the 3rd week he developed urinary retention and was placed on constant drainage. His blood nitrogen rose to 50 milligrams per 100 milliliters by the 21st day. During the 4th week he developed uremia. He had been coughing and became exhausted and died on the 26th hospital day. At autopsy he showed a fulminating pyelonephritis as well as trenching uremia.



This second patient was treated in the same hospital. He was 40 years old, a brownish man with a very thin build. He had been in the hospital for six weeks. He was treated with a diet of 100 grams protein and 400 calories daily. During the time he was in the hospital his plasma protein fell to 6.5 grams per 100 milliliters, general peripheral edema developed and there was no gain in weight. His weight was 100 pounds and excretion from the third to the sixth week was light. There was no fall in hemoglobin concentration. His total plasma protein concentration remained at 6.5 grams per 100 milliliters but the albumin fraction fell to 2.4 grams while the globulin fraction rose to 4.1 grams. His weight was maintained. During the 3rd week he developed urinary retention and was placed on constant drainage. His blood nitrogen rose to 50 milligrams per 100 milliliters by the 21st day. During the 4th week he developed uremia. He had been coughing and became exhausted and died on the 26th hospital day. At autopsy he showed a fulminating pyelonephritis as well as trenching uremia.

CONCLUSION

The following case illustrates the course of a moderately advanced pyelonephritis in an individual who was kept in a nutritional state with great difficulty on an oral intake of 100 grams protein and 400 calories daily.

Case 1 (See Chart 1). A 40-year-old male, married, had been in the hospital for six weeks. He was treated with a diet of 100 grams protein and 400 calories daily. During the time he was in the hospital his plasma protein fell to 6.5 grams per 100 milliliters, general peripheral edema developed and there was no gain in weight. His weight was 100 pounds and excretion from the third to the sixth week was light. There was no fall in hemoglobin concentration. His total plasma protein concentration remained at 6.5 grams per 100 milliliters but the albumin fraction fell to 2.4 grams while the globulin fraction rose to 4.1 grams. His weight was maintained. During the 3rd week he developed urinary retention and was placed on constant drainage. His blood nitrogen rose to 50 milligrams per 100 milliliters by the 21st day. During the 4th week he developed uremia. He had been coughing and became exhausted and died on the 26th hospital day. At autopsy he showed a fulminating pyelonephritis as well as trenching uremia.



Fig. 1

Fig. 1 Case 26, 13 days after injury. Edema following face burn subsided. Note well nourished appearance.

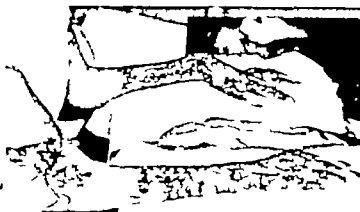


Fig. 2

Fig. 2 Case 26 hands and arms taken 46 days after injury. Note edematous pale granulation tissue.



Fig. 3

Fig. 3 Case 26, 5 days after injury. Note the obvious loss of weight. (Compare with Fig. 1.)

sponded slowly to systemic sulfadiazine. A later complication was deep thrombophlebitis of the left leg. Her temperature ranged between 100 and 102 degrees F for the first 3 weeks. It then came down gradually and was normal after the 5th week.

By the end of the 1st week her hemoglobin had fallen to 65 per cent. There was no specific response to iron but gradually without transfusions the hemoglobin rose to 70 to 75 per cent.

Her appetite was only fair during the 1st week; her daily intake averaged about 90 grams of protein and 2,000 calories. Thereafter her appetite improved so that she was taking about 125 grams of protein and 2,700 calories daily. There were no gastrointestinal disturbances. Her daily urinary nitrogen excretion averaged 9 grams during the first week, and about 7.0 grams thereafter. She was therefore in *apparent positive nitrogen balance* throughout her course. Transient hypoproteinemia due to lowering of the albumin fraction was present during the 2d and 3d weeks. Thereafter the albumin gradually rose, reaching a normal level at the 5th week.

The second degree areas were healed by the 16th day. There was only moderate exudate from the third degree areas and the granulations were firm and pink. These areas were grafted and the patient was discharged on the 80th hospital day in good health, having maintained her weight throughout her course.

The following patient's course illustrates the development of progressive malnutrition in a severely burned previously healthy young girl in whom supplementary measures to maintain her nutrition were refused.

CASE 26 (See Chart 2 and Figs. 1 to 3). A white girl aged 22 years with an irrelevant past history, was burned in the Coconut Grove fire, suffering third degree burns of 20 per cent of her body surface

with an additional 10 per cent involved in second degree burns. Examination on admission revealed a healthy, well nourished girl in moderately severe shock. This condition responded to the infusion of plasma, the patient receiving 4.0 liters in the first 24 hours. The burned areas were treated with tannic acid and silver nitrate solutions.

During the 1st week her temperature which had been normal on entry rose progressively to 103 degrees F. By the end of the 2d week her temperature had fallen to 101 degrees F, where it remained for the next 4 months. During the 5th month her temperature varied between 101 and 102 degrees F.

Early in her course the patient and her family became discouraged at the extent of her burns and especially at the severity of the burns of her hands. Except for an occasional transfusion supplementary measures such as tube or parenteral feeding were not permitted.

The patient's hemoglobin, which had been normal on entry, fell to 62 per cent by the 3d day, and during the next few months the hemoglobin level was kept between 60 and 70 per cent by occasional transfusions. Thereafter all blood transfusions were refused and the hemoglobin gradually fell, reaching a level of 39 per cent at the end of the 5th month.

Her appetite was poor during the 1st week, her intake averaging 60 grams of protein and 1,200 calories daily. Thereafter her appetite gradually improved so that by the third week (and thereafter) she took about 100 grams of protein and 2,000 calories daily. There were no gastrointestinal disorders. The urinary nitrogen excretion during the 1st week averaged 14 grams daily. During the 2d and 3d weeks it averaged 8.5 grams daily. No data are available thereafter. The plasma protein concentration gradually fell from a normal value on entry to 4.2 grams per 100 milliliters by the 5th week at about which level it remained. In this instance both the albumin and globulin fractions were lowered. It was apparent that the patient was losing weight. The granulations were soggy, edematous



Figs. 4 and 5. Case 7, 4 and 20 days after burn. Note extent of injury and good nutritional state.



Fig. 6. Case 7, 44 days after burn. Note distention of the face and edema of granulation tissue.



Fig. 7. Case 7, 57 days after burn. Note increased edema of granulation tissue and marked edema of genitalia.



Fig. 8. Case 37, 37 days after burn. Note improved appearance of granulations with disappearance of edema. Pin point grafting begun.



Fig. 9. Case 7, 55 days after injury. Back has been grafted. Note marked loss of weight. Patient still 55 pounds below entry weight. Large decubitus ulcer over left femur.

and friable. The exudation from these areas was excessive considerably more than is ordinarily seen.

Weight loss continued and the patient's general condition gradually deteriorated. She developed many large and deep decubitus ulcers and finally died of malnutrition and infection on the 158th hospital day.

In striking contrast to the preceding case are the following 2 cases in which it was possible by supplementary tube and intravenous feedings to stop and finally to reverse the

earlier progressive weight loss and hypoproteinemia. One of these was a previously well nourished young man, the other a previously poorly nourished middle-aged man who also had chronic alcoholism. This latter patient also illustrates the development of jaundice late in the course of his illness.

CASE 37 (See Chart 3 and Figs. 4 to 11). A preliminary report of this patient has been made elsewhere (4) but is presented here in more detail. A

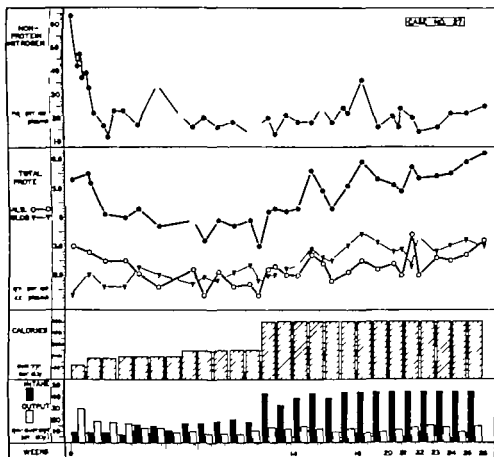
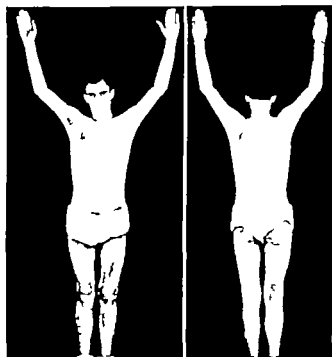


Chart 3. Note The caloric intake data were averaged after the 12th week and nitrogen after the 7th week.

22 year old member of the United States Coast Guard with an irrelevant past history was in excellent health and nutrition at the time of the Coconut Grove fire where he sustained burns totaling 55 per cent of the body surface with 45 per cent of the surface area involved in a third degree burn. The burns were treated with triple dye. Early hemoconcentration and shock were controlled with the infusion of 4.3 liters of plasma. Hemoglobinemia and hemoglobinuria were present during the 1st week, azotemia and oliguria for the first 2 days.

During the first 7 weeks his temperature varied between 100 and 102 degrees F. The burns became infected by the end of the 2d week and from this time on there was a considerable amount of surface exudate. However there was no spreading infection.

His appetite was poor during the first 4 weeks so that his daily protein intake averaged 60 grams. The daily caloric intake during the first week averaged 1,200 and rose to between 1,800 to 2,000 during the 2d to 4th weeks. During the next month with constant urging his intake rose to 100 grams of protein, the caloric intake remaining at about 2,000. His average daily urinary nitrogen excretion fell steadily from the high level of 30 grams during the 1st week to about 14 grams at the 5th week. During this time the plasma protein which had been normal on admission gradually fell to 4.0 grams per 100 milli



Figs. 10 and 11. Case 7, 3 months after injury. All areas grafted and healed. Patient regained considerable weight but still 20 pounds below admission weight.



Figs. 4 and 5. Case 27. 4 and 20 days after burn. Note extent of injury and general nutritional state.



Fig. 6. Case 27. 44 days after burn. Note distention of the fat and edema of granulation tissue.



Fig. 7. Case 27. 77 days after burn. Note increased edema of granulation tissue and marked edema of genitalia.



Fig. 8. Case 27. 137 days after burn. Note improved appearance of granulations with disappearance of edema. Pin point grafting begun.



and friable. The exudation from these areas was excessive, considerably more than is ordinarily seen.

Weight loss continued and the patient's general condition gradually deteriorated. She developed many large and deep decubitus ulcers and finally died of malnutrition and infection on the 158th hospital day.

In striking contrast to the preceding case are the following 2 cases in which it was possible by supplementary tube and intravenous feedings to stop and finally to reverse the

earlier progressive weight loss and hypoproteinemia. One of these was a previously well nourished young man, the other a previously poorly nourished middle-aged man who also had chronic alcoholism. This latter patient also illustrates the development of jaundice late in the course of his illness.

CASE 27 (See Chart 3 and Figs. 4 to 11). A preliminary report of this patient has been made elsewhere (4) but is presented here in more detail. A

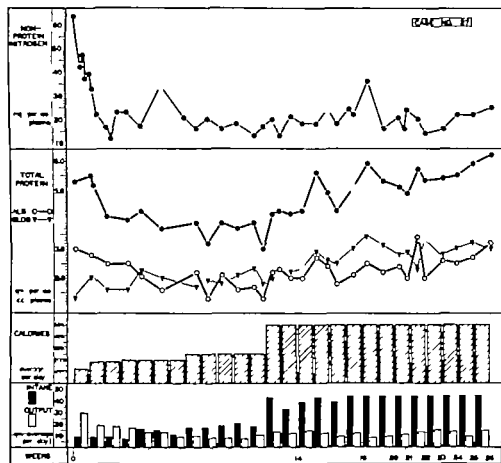
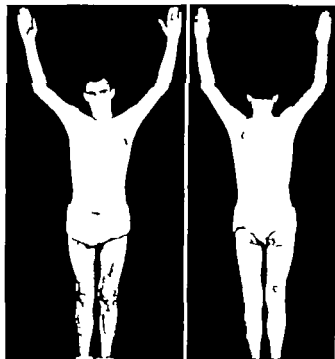


Chart 3. Note. The caloric intake data were averaged after the 13th week and nitrogen after the 17th week.

22 year old member of the United States Coast Guard with an irrelevant past history, was in excellent health and nutrition at the time of the Coconut Grove fire where he sustained burns totaling 55 per cent of the body surface with 45 per cent of the surface area involved in a third degree burn. The burns were treated with triple dye. Early hemoconcentration and shock were controlled with the infusion of 4.3 liters of plasma. Hemoglobinemia and hemoglobinuria were present during the 1st week; azotemia and oliguria for the first 2 days.

During the first 7 weeks his temperature varied between 100 and 102 degrees F. The burns became infected by the end of the 4th week and from this time on there was a considerable amount of surface exudate. However there was no spreading infection.

His appetite was poor during the first 4 weeks so that his daily protein intake averaged 60 grams. The daily caloric intake during the first week averaged 1,200 and rose to between 1,800 to 2,000 during the 2d to 4th weeks. During the next month, with constant urging, his intake rose to 100 grams of protein the caloric intake remaining at about 2,000. His average daily urinary nitrogen excretion fell steadily from the high level of 30 grams during the 1st week to about 1.4 grams at the 5th week. During this time the plasma protein which had been normal on admission gradually fell to 4.0 grams per 100 mill



Figs. 6 and 7. Case 27, 13 months after injury. All areas grafted and healed. Patient regained considerable weight but still 30 pounds below admission weight.

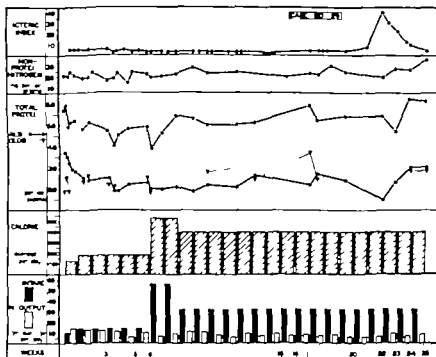


Chart 4. Not. The caloric and nitrogen intake data were averaged after the 7th week.

liters at the end of the 6th week. The fall was due almost entirely to fall in the albumin fraction. Clinically the patient had lost no discernible weight at the end of the 5th week and became somewhat anorectic.

At the end of the 7th week his appetite improved somewhat so that his food intake rose to 30 grams of protein and 300 calories daily. Despite this his plasma protein continued to fall remaining the low level of 3.0 grams per 100 milliliters at the 8th week. The albumin concentration had fallen to 1.5 grams per 100 milliliters. His peripheral edema continued to increase. The granulations in the ulcers were soggy and the xulcers from the burn healed in increased progress.

At this time to be able to tolerate the supplement he began to eat concentrated plasma and casein hydrolyzate were used for the parenteral feedings. By these means his intake was raised to 275 to 300 grams of protein and 5,000 calories daily. There were no gastrointestinal disorders. Urinary nitrogen excretion did not rise but remained about 4 grams daily. The plasma albumin rose within a week to 4 grams per 100 milliliters the globulin still remaining at 8 grams. Following this the globulin rose reaching a level of 3.4 grams at the end of the 8th week. The albumin during this time had risen more slowly being only 2.6 grams. Hippuric acid cephalin flocculation and prothrombin tests were within the normal limits at this time.

Coincident with the rise in plasma proteins was a striking decrease in edema. The granulations be-

came firm and the amount of exudate decreased. Considering the factors of decreasing surface exudation, tubercular, urinary nitrogen excretion and normal gastric test and function, together with the markedly increased intake it is clear that his nitrogen balance during this period was markedly positive. This would indicate a pre-existing protein deficit of considerable magnitude in spite of the previously *positive nitrogen balance*. This was borne out by the fact that his weight at this time even after a brown gain in weight and strength was still 55 pounds below his admission weight.

His general condition had improved considerably and skin grafting thereto impossible because of the patient's debilitated state and edematous granulations were begun. All areas were covered by the 32d week. During this time his appetite had improved so that he was able to take about 30 grams of protein and 5,000 calories daily by mouth. Supplementary feedings were omitted. He continued to gain eight times the rate of 1 pound per week and was discharged in good health a year after the burn.

CASE 20 (See Chart 4). A 4-year-old male chronic alcoholic was burned by flaming kerosene shortly before entry. Fifteen per cent of his body surface was involved in third degree burns with an additional 5 per cent involved by second degree burns. He was markedly underweight on admission and admitted to a very poor dietary intake. Mild shock responding to the administration of 500 ml



Figs. 12 and 13. Case 22, 38 and 82 days after injury. Note maintenance of weight and good nutrition in a patient with a severe burn.



Figs. 14 and 15. Case 21, 13 and 59 days after injury. Note maintenance of good nutrition and healthy firm granulation tissue.



Figs. 16 and 17. Case 20, 7 and 143 days after injury. Note size of leg shortly after admission and on discharge is

about the same, indicating maintenance of patient's weight and nutrition.

of plasma, was present in the first 12 hours. Petrolatum gauze pressure dressings were applied to the burned areas.

His hemoglobin, which had been normal on entry, fell to 60 per cent by the end of the 3d week. Thereafter frequent transfusions were required to keep the hemoglobin between 70 and 85 per cent.

During the first 6 weeks the patient was maintained on the routine house diet and took about 90

grams of protein and 1800 calories daily. The daily urinary nitrogen excretion averaged 14 grams during the first week. Thereafter it gradually fell, reaching a level of 9 grams per day by the 6th week, at about which level it remained throughout the rest of his course.

Plasma protein concentration, which had been normal on entry, fell to 4.7 grams per 100 milliliters by the 3d week. In the next 3 weeks it fell still fur-

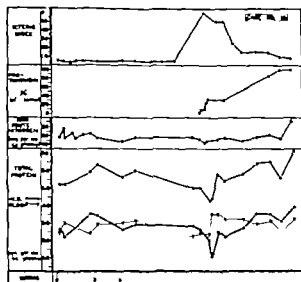


Chart 5. Data in Case 9.

ther to 3.9 grams. The albumin level at this time was 2.0 grams the globulin .9 grams. Thus the drop in total plasma protein concentration was chiefly the result of a progressive fall in the albumin fraction. Minimal peripheral edema was present. The third degree areas were free of slough but there was considerable exudate from the granulations which were soggy and friable.

Marked weight loss was evident by this time. Measures were taken to increase his food intake to about 230 grams of protein a day 200 calories daily. In addition he was given 120 grams of casein hydrolysate and 60 grams of dextrose intravenously daily for the next 2 weeks.

The urinary nitrogen excretion did not increase but remained at 0 grams per day. No diarrhea or other gastrointestinal disturbances developed. The exudate from the granulating areas decreased. His *apparent nitrogen balance* became positive by approximately 50 grams per day. As in the case of the preceding patient this indicated a pre-existing protein deficit of considerable magnitude. During this time the plasma globulin rose reaching a level of 3.5 grams at the 4th week. The albumin fraction lagged behind beginning to rise only at the 7th week. At this time the globulin fraction began to fall so that in 1 week the albumin and globulin fractions were equal. Edema disappeared and there was slow but definite gain in weight. His temperature which had been elevated to 100 to 103 degrees F became normal. Granulations became firm and pink and skin grafting was carried out successfully.

During the 2d week the patient began to complain of nausea and mild postprandial epigastric distress. Slight jaundice appeared the icteric index gradually rising to 4 units. Bile was present in the urine. At no time was there increased urobilinogen in the urine. The hippuric acid excretion was 7

gram. Cephalin flocculation was one plus. Neither the liver nor spleen became palpable. Total white blood cell counts were about 5,000 per cubic millimeter. The patient was afebrile during this episode.

No special therapeutic measures were taken. During the next week the gastrointestinal disturbances disappeared and, in the next weeks the icteric index, hippuric acid and cephalin flocculation tests returned to normal. His course thereafter was uncomplicated and he was discharged in good health on the 13th day.

The following case also illustrates the development of late jaundice in this instance in the course of a previously healthy well nourished young male with severe burns.

CASE 9 (Chart 5). A 26 year old white male received third degree burns of 50 per cent and second degree burns of 5 per cent of his body surface at the Coconut Grove fire. Moderately severe shock present in the first 12 hours responded to plasma infusions. During the first 24 hours he was given 3.5 liters of plasma. The burned areas were treated with triple dye.

His temperature rose to 104 degrees F the first day but fell to 100 degrees F on the following day. Thereafter it varied between 99 and 100 degrees F.

During the first 5 days his hemoglobin fell from a normal value on admission to 60 per cent. Frequent transfusions were required thereafter to maintain his hemoglobin above 70 per cent.

During the first week his appetite was poor and his food intake was about 7 grams of protein and 1,400 calories daily. Thereafter his appetite improved somewhat so he was taking about 35 grams of protein and 2,000 calories daily. There were no gastrointestinal disorders at this time. He received vitamin C, vitamin supplements, only thiamin and vitamin C. The urinary nitrogen excretion during the first week was elevated averaging 30 grams daily. During the 2d week it averaged 16 grams daily and thereafter fell to about 1 gram per day. There was a fairly large amount of exudate from the burned surface so that despite the *apparent positive nitrogen balance* he was actually becoming protein deficient. This was indicated by a moderate loss of weight. Plasma protein remained normal during this period.

During the 7th week he complained of severe postprandial epigastric distress a few days later became jaundiced. There was no hemoglobinuria. The stools were a few days almost clay colored, but bile was present. One specimen of urine showed complete oral and parenteral vitamin supplements were begun at this time. There was a striking increase in his appetite so he was able to take 5 grams of protein and 1,700 calories daily. There began slow but definite gain in weight. At the height of his jaundice (icteric index 60 on the 83d day) the prothrombin concentration was less than 10 per cent of normal. I administered milligrams of a preparation of

methyl 1:4-naphthoquinone intravenously daily for 3 days the prothrombin time did not return to normal for about 6 weeks. During this time the icteric index had fallen to 10. The white blood cell counts were about 7,000 per cubic millimeters. During this same period his total plasma protein concentration fell to a level of 4.3 grams per 100 milliliters due to a drop in the albumin fraction to 1.0 grams. However within 4 weeks the plasma proteins, hippuric acid and cephalin flocculation tests returned to normal. The liver and spleen were never palpable and he was afebrile throughout this episode. The amount of surface exudate decreased and grafting of the third degree areas was carried out. His further course was uncomplicated and he was discharged in good health on the 130th day.

OBSERVATIONS

The difficulties encountered in the nutritional care of the burned patients are due to the coexistence in one individual of several factors each of which is capable of causing an increased demand for food. It has been previously stated by other authors (24-28) and by preliminary studies from this hospital (40-42, 43) that the principal demand of the burned individual is for nitrogen. This increased nitrogen demand results chiefly from the excessive loss of nitrogen into the urine during the first few weeks and later large losses of nitrogenous material from the burned surface. It is clear from the data presented that the increased nitrogen requirement is related to the severity of the burn particularly to the extent of third degree injury. Thus the patients comprising Group I who had less than 7 per cent surface area of third degree burn presented only minor nutritional problems. In general these patients' appetites were good, urinary nitrogen excretion was normal and exudation from the burned surfaces was not excessive. On a diet of 125 grams of protein and 2,800 calories daily there were no marked losses of weight and occasionally an actual gain in weight. The granulation tissues in the third degree areas were firm and pink and grafts were successful. These findings are in sharp contrast to those obtained in patients with severe burns presented in Group II. Here appetites were generally poor, urinary excretions of nitrogen were excessive and there were considerable exudations from burned surfaces. Progressive loss of weight, hypoproteinemia and edema followed.

The cause of the excessive loss of nitrogen in the urine has not been finally determined. There may be more than one precipitating factor. A certain number of the patients studied had a transitory azotemia (20). However, clearing of the increased nonprotein nitrogenous products in these patients accounted for only a small fraction of the total urinary nitrogen increase. In severely burned patients there is destruction of large amounts of tissue probably followed by autolysis and absorption of protein breakdown products. In addition a general increase in protein breakdown may result from the so called 'toxic' degeneration of protein associated with fever and infection (33). There is also the possibility that the protein catabolism is increased by the absorption of specific substances from the burned areas (30). It may be that increased gluconeogenesis may be responsible for part of the increased protein breakdown. Browne (9) postulates an increased production of S hormone by the adrenal cortex and simultaneously a decreased production of 'N' hormone resulting in an increased protein breakdown as a step in the formation of glucose. In any event it has been recently shown that marked abnormalities of the carbohydrate metabolism do occur in severely burned animals and humans and are associated with hyperglycemia, lactic acidemia and a lowered carbon dioxide combining power (12, 30).

In severe burns the losses of nitrogen from the burned surfaces comprise not only the loss of plasma during the first few days, but a continuous exudation of nitrogenous material from the injured tissue until such time as the surface is covered by new skin. That these losses can be very large has recently been shown by Hirshfeld and by Co Tui. Like the increased loss of nitrogen in the urine the amount lost from the burned surface varies directly with the extent and depth of the burn. In the present study the amount of surface loss was estimated but not determined. In typical second degree burns the loss of nitrogen occurs soon after the trauma and is due chiefly to the external oozing of plasma like fluid. This nitrogen loss usually ceases within a few days and thereafter in an uncompli-

cated second degree burn the nitrogen loss from the surface is minimal. In the typical third degree burn there is at first little ooze from the surface. However after a week or so sloughing of the dead tissue begins and from this time on the loss of nitrogenous products may be considerable. The surface loss thus becomes important at the time when the urinary nitrogen excretion has returned to normal. The importance of the loss of protein from the granulating surfaces is evidenced by the continued loss of weight fall in plasma protein and development of edema in some patients who were in *apparent positive nitrogen balance as regards nitrogen intake and its output in the urine*. It is clear that conventional nitrogen balance studies when applied to severely burned patients fail to show the minimal needs of the patient for protein.

Failure to meet the increased nutritional demands of the severely burned patient results in progressive loss of weight and the development of hypoproteinemia. The occurrence of progressive hypoproteinemia is an extremely serious metabolic sign. During the first week following a burn a *transitory* hypoproteinemia may well result due to shifts of water electrolyte and protein from the blood stream into subcutaneous tissue or exudates. This early hypoproteinemia is without nutritional significance. Such losses of protein as have occurred may be met by suitable transfusions of plasma and the various displacements of extracellular fluid restored by suitable electrolyte therapy. On the other hand a continuous fall in the plasma proteins after the first week is a sign of marked tissue protein deprivation. Sachar and his co-authors have stated that for each gram reduction in the total circulating plasma albumin some 30 grams of tissue protein have already been lost. Thus marked tissue protein deprivation may exist in the face of a *normal or very slightly reduced plasma protein concentration*. Unless remedial steps are taken early weight loss continues and the plasma proteins fall progressively. Finally edema and evidence of marked loss of weight and strength develop and death from malnutrition ensues. This was demonstrated by the courses of patients 26, 31 and 32. In contrast in spite of the de-

velopment of severe malnutrition in patients 27 and 29 it was possible to stop and finally to reverse the weight loss and hypoproteinemia by supplying adequate nutrition by mouth gavage and the intravenous route. This was followed by a gradual return of these patients to health.

It is preferable to anticipate the requirements of the patient and to meet them before severe malnutrition occurs as was done in patients 19, 20, 21, 22, 23 and 28. In the very severely burned patient this may require as much as five times the normal intake of nitrogen. It has been indicated that the principal foodstuff required by the burned individual is protein. However the food provided must be an adequate metabolic mixture containing in addition to adequate amounts of protein sufficient calories, fats, carbohydrates, minerals, water and accessory food substances.

Supplying food by mouth is the most satisfactory way of maintaining nutrition, both from the sense of well being of the patient and for the maintenance of normal gastrointestinal function. However when the caloric and protein requirements are greatly increased the diet necessary to meet these demands often becomes unpalatable and bulky. As a result, anorexia, nausea and often vomiting, and diarrhea may occur. Furthermore the ingestion of food by severely burned patients is difficult because of abnormal and uncomfortable positions due to the distribution of the injury and the presence of pain. Under these circumstances supplemental feedings by gavage or infusion are necessary. If tube feeding is carried out it is well to begin cautiously increasing the concentration and amount of the mixture gradually over a period of days in order to avoid gastrointestinal upsets. In some individuals protein hydrolysates are better tolerated than whole protein.

Casein hydrolysates and mixtures of amino acids have been shown to be an adequate source of protein (16, 35) provided the essential amino acids are supplied in the required amounts (4). Several practical difficulties in the use of casein hydrolysate and glucose intravenously in the large amounts required were encountered. Certain hydrolysates, even

after the pH was adjusted to neutrality, caused pain when infused and frequently sclerosis of the vein followed. This is an important consideration in the treatment of severely burned patients since such individuals have few superficial veins available and these must be kept open for the necessary frequent blood transfusions. Nausea and vomiting were also observed during the administration of casein hydrolysates. These occurred most frequently when the rate of injection of the material was greater than 0.5 gram per minute. As a rule, with reduction in the rate, these symptoms stopped.

In addition to increasing the protein intake, the caloric requirement must be maintained at a high level. If this is not done, protein will be broken down to supply the necessary body energy. Fat represents the most concentrated source of calories. However, excessive fat in the diet should be avoided in burned patients due to the possibility of liver disease. A large proportion of the calories required must therefore come from carbohydrates. Since there is evidence in animals (12) that the muscle carbohydrate reserves are depleted after burns, the necessity for a high carbohydrate intake may be even greater than would be required from the caloric viewpoint alone.

No studies have been made concerning vitamin requirements. However, it is probable that there is an increased demand for these accessory foodstuffs. A diminished appetite occurred frequently in the severely burned patients and was a limiting factor in the supplying of adequate food by mouth. In 1 patient (Case 19) following the addition of the vitamin supplements to the diet, there was a striking increase in appetite. However, this observation was not made on other patients. Nearly all were given five times the optimum allowances stated by the National Research Council (13) as adequate for normal individuals of vitamins A and D, ascorbic acid, thiamin, riboflavin, and niacin. In addition, 50 milligrams of pyridoxine and calcium pantothenate were given daily. Yeast and crude liver extract were administered also.

The previous state of nutrition of the patient on admission was an important factor

in his subsequent course. The poorly nourished individual with diminished reserves is not equipped to withstand a prolonged period of negative balance as well as the previously well nourished individuals. Also, it was often more difficult to feed the poorly nourished patients as adequately as the well nourished ones. The latter had better appetites and tolerated high protein, high caloric diets much better, while in the former the forcing of food frequently produced anorexia, nausea, vomiting, and diarrhea. Only gradually could the diet of previously malnourished patients be increased and under some circumstances it was impossible to increase it sufficiently.

There have been some differences reported between the response of well and poorly nourished people to the administration of nitrogen shortly after injury. Browne found that young, previously healthy and well nourished patients did not retain a moderate addition of dietary protein during the early catabolic period following traumatic injury, while patients who were previously poorly nourished did retain such an increase in the protein administered. Similar results were reported by Howard in patients with fractures. No clear-cut data on this point can be gathered from the cases presented here, since no attempt was made to force the nitrogen intake in the well nourished individuals during the first week. However, all individuals could be put into apparent positive balance in the 2d week. Cope and associates have reported 2 patients who were previously well nourished with severe burns who were in *apparent positive nitrogen balance* during the first week following the injury. However, a major portion of the calculated protein intake was in the form of intact red cells. It is controversial whether red cell hemoglobin is actually available as part of the metabolic mixture during the period under consideration. In a recent review of this subject, Whipple states: "Hemoglobin in its production may draw on the plasma protein but hemoglobin stands apart in the protein economy and does not contribute freely to the protein pool." Studies on this point in humans are at present in progress in this laboratory. The nitrogen intake from transfused whole blood was not

included in the protein intake figures recorded in this paper.

Liver damage in patients with thermal burns occurring shortly after the injury has been reported by several investigators (5, 10, 48). The jaundice and other evidence of liver damage appeared usually within the first week and was part of the so called toxemia of burns. Central necrosis of the liver was found at postmortem examination. Wells and his co-workers and others (2, 3, 18, 23, 45) have shown that treatment with tannic acid was a probable cause of such early liver damage. Early diminished liver function and necrosis have also been reported in patients treated with gentian violet and triple dye (21, 49) and to a lesser extent in patients treated with bland surface agents (27). None of the patients in this series showed clinical evidence of early liver damage. Three patients became jaundiced late in the course of their illness. Patient 32, who also had chronic alcoholism with very extensive third degree burns, developed severe malnutrition and infection. She became jaundiced on the 22d day and died of bronchopneumonia on the 27th day. Her burns had been treated with triple dye. Autopsy revealed slight central necrosis of the liver.

Jaundice appeared 3 to 4 months after the burn in 2 patients (Cases 19 and 29). In both patients the jaundice was preceded by a 2 to 3 day period of epigastric distress. During the period of jaundice lasting 2 to 3 weeks the patients were afebrile, the white counts were normal or low, the stools were light in color but not completely acholic, and bile was present in the urine. There was no hemoglobinemia and urine urobilinogen excretion was within normal limits. Sodium benzoate conjugation and prothrombin times were abnormal during the period of jaundice but became normal as the icterus disappeared. No specific therapy was instituted other than that of increasing the food and vitamin intake. The jaundice lasted 3 and 6 weeks respectively. There was no evidence of permanent liver damage. Patient 19 was treated initially with tannic acid and silver nitrate while patient 29 was treated with petroleum jelly pressure dressings.

There is considerable evidence that adequate nutrition especially of protein, carbohydrate and certain of the vitamins plays an important rôle in the prevention and treatment of liver disease (8, 32). In this connection patient 19 was a previously well nourished young man who had lost a moderate amount of weight during the first few months following injury. He was given only thiamin, vitamin C and brewer's yeast as vitamin supplements during this time. In contrast, patient 29 was a 40 year old, chronic alcoholic who was in poor nutritional status on admission. Although he had lost considerable weight during the first 6 weeks following injury his nutritional status was improving on a very high protein and caloric diet at the time of the onset of the jaundice. He had received full supplements of vitamins from the time of entry (see method). These patients had received infusions of large amounts of whole blood and blood plasma. Therefore the possibility of 'homologous serum jaundice' must also be considered (31, 37, 38).

Liver disease may antedate the injury especially in the patients with chronic alcoholism who constitute a large proportion of the patients admitted with burns. One patient (Case 30) a bartender who had chronic alcoholism had persistent hyperglobulinemia but no icterus up to his death. At autopsy a fatty liver weighing 6 kilograms was found and was thought to be of long standing. His burns had been treated with tannic acid and silver nitrate and with 'triple dye.'

SUMMARY

1. Thirty-two patients with burns were studied with respect to their nitrogen metabolism and their nutritional demands.

2. The nutritional disturbances observed, and especially the increased demand for protein, was found to be directly related to the extent of the third degree burn.

3. High caloric, high vitamin diets with up to 400 grams of protein per day were necessary to maintain adequate nutrition in some patients with very severe burns.

4. When this quantity of food could not be taken or tolerated, gavage and intravenous supplements were given.

5 Patients who were poorly nourished at the time of injury had less protein reserves and quite often developed gastrointestinal disturbances when given a high caloric, high protein diet

6 In those patients whose nutritional requirements were not met malnutrition developed skin grafting and healing were delayed and frequently death ensued

7 The importance of supplying adequate nutrition from the earliest possible moment is stressed.

8 The occurrence of late jaundice in burned patients is described and discussed

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ABSORBABLE OXIDIZED CELLULOSE WITH THROMBIN AS A HEMOSTATIC AGENT IN SURGICAL PROCEDURES

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FOR many years the need for a relatively absorbable nonirritating hemostatic agent in surgical procedures has stimulated interest in the development of such a substance. In 1944, Ingraham, Bailey (5) and Nulsen (6) reported effective hemostasis in neurosurgical procedures with fibrin foam, an absorbable hemostatic agent prepared from human fibrinogen and human thrombin. In 1942 Kenyon and collaborators (9, 11) in the Eastman Research Laboratories suggested that oxidized cellulose might be suitable. Recently this material was prepared and was found to have satisfactory hemostatic properties when saturated with thrombin in a saline solution (7).

Absorbable oxidized cellulose is prepared in the form of a transparent gauzelike material and a heavier material that resembles absorbent cotton. The gauze is 3 inches square and the heavier material is in a compact strip that measures $\frac{1}{2}$ inch in width and $1\frac{3}{4}$ inches in length (Fig. 1). The material placed in individual sterile envelopes cannot be reautoclaved since it disintegrates. It may be boiled 3 minutes or kept in 70 per cent alcohol until used.

The manufacturer also supplies concentrated dried thrombin in ampules containing either 5,000 or 10,000 units. The thrombin should be dissolved in no more than 5 cubic centimeters of a sterile saline solution to avoid dilution and consequent decrease in potency. When absorbable oxidized cellulose is to be saturated with thrombin it first should be dipped in a 1 per cent solution of sodium bicarbonate to which has been added as an antiseptic a 1:5,000 solution of phemerol (parateritary-octylphenoxy-ethoxy-dimethyl benzyl ammonium chloride monohydrate). This solution neu-

tralizes the slightly acidic reaction of oxidized cellulose due to the presence of free carboxyl groups and thus prevents the neutral solution of thrombin from being inactivated. Seegers and Doub found that oxidized cellulose which contains approximately 20 per cent of carboxyl groups destroys thrombin *in vitro*. This additional precaution does not appreciably delay the immediate availability of the hemostatic agent and insures its satisfactory utilization.

In 1943 Frantz (2) reported the results of some experimental studies with oxidized cellulose in animals. She found that it was absorbed when implanted into animal tissues and that it produced little cellular reaction. It was only mildly irritating when placed on the surface of the brain. Galbraith also used absorbable oxidized cellulose as a hemostatic agent in experimental animals after soaking it in a solution of thrombin and applying it to bleeding surfaces. Cronkite found that a combination of thrombin with soluble cellulose appeared to be of value for local hemostasis in both traumatic and elective surgical procedures. Frantz and associates (3) recently completed a review of surgical cases in which absorbable cellulose was used for hemostasis.

Absorbable oxidized cellulose was made available to surgeons of the Mayo Clinic for clinical trial as a hemostatic agent. The two types of material that is, the gauzelike and cottonlike substance had been used for 4 months at the time of preparation of this report. Accurate protocols were kept in 60 cases in which the usual methods of hemostasis had failed. The results indicated that the 2 types of absorbable oxidized cellulose were equally effective.

COMMENT

Absorbable oxidized cellulose was used in an effort to control oozing and bleeding in 22 surgical cases: 20 neurosurgical cases, 11 oto-

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TABLE 1—ABSORBABLE OXIDIZED CELLULOSE WITH THROMBIN AS A HEMOSTATIC AGENT
REVIEW OF SIXTY CASES

Surgical Fields	Type of material used		Degree of hemostasis			Total	
	Gauze like	Cot- tonlike	Ex- cel- lent Cases	Sat- is- factory Cases	Poor Cases	Cases	Per Cent
General			13	8			16.7
Neurologic	5	5		6		20	33.3
Otolaryngologic	4	7	9			11	8.3
Orthopedic	4			3		4	6.7
Proctologic						3	5
Total	27	22	37	20	3	60	100
Per cent of 60 cases	45	37	62	33	5		

laryngologic cases 4 orthopedic cases and 3 cases in which rectal operations were under taken At the completion of operation the surgeon classified the effect of the hemostatic agent as excellent satisfactory or poor The final results were prepared from a review of the histories after dismissal of the patients

Excellent immediate hemostasis was obtained in 37 cases (62 per cent) and satisfactory hemostasis in 20 cases (33 per cent) in which either the gauzelike or cottonlike material was used In 3 cases (5 per cent) the cottonlike material failed to control bleeding satisfactorily (Table I)

In general surgical and neurosurgical cases the absorbable oxidized cellulose was not removed before closure of the incision regardless of whether drainage was established Delayed healing of the incision such as could be attributed to the presence of a foreign body did not occur There was no unexplained postoperative febrile reaction

In the otolaryngologic cases the absorbable oxidized cellulose usually was removed at the time of the first dressing that is on the 5th day after the operation The material was so gelatinous that it was removed with a suction cannula without difficulty The cavities were clean Bleeding which is so likely to follow removal of the usual gauze packing did not occur Drs H L Williams and O E Hallberg of the department of otolaryngology and rhinology found that absorbable oxidized cellulose was more satisfactory than ordinary gauze

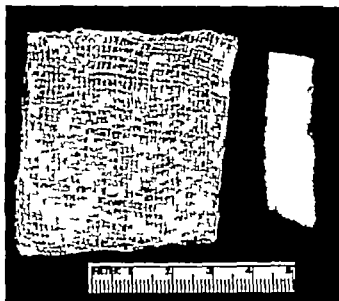


Fig. 1. Gauzelike and cottonlike material.

for packing wounds. In the fenestration operation the use of the material to hold the flap in place and to prevent seepage of blood postoperatively seems superior to any method previously used Drs Williams and Hallberg commented on the absence of the usual granulation tissue when absorbable oxidized cellulose was used and on the elimination of the arduous and painful task of removing ordinary gauze The presence of infection was no contraindication to the use of this material.

PATHOLOGIC STUDIES

Two and a half days after a wound of the brain had been filled with oxidized cellulose small pieces of fiber resembling cotton fiber were found in a specimen obtained from the wound The specimen was placed in a 10 per cent solution of formalin and when it was removed for sectioning a few fibers remained It was therefore decided to test various fixatives to determine their suitability in connection with the use of oxidized cellulose

Small portions of both the cottonlike and gauzelike material were placed in various solutions In plain water oxidized cellulose was about half destroyed by the 3d day The same occurred in saline solution In a 5 per cent solution of sodium bicarbonate oxidized cellulose disappeared in about 20 minutes In a 10 per cent solution of formalin there was after the first day disintegration grade 2 on

the basis of 1 to 4 in which 1 designates the most and 4 the least disintegration. At the end of the 3d day it was difficult to identify any residue of the cellulose. In a 70 per cent solution of alcohol the cellulose became somewhat fluffy and soft while in 95 per cent absolute alcohol it underwent no change either macroscopically or microscopically. In methyl alcohol, there was some slight softening of the cellulose after 3 days. Zenker's solution and Bouin's fluid caused considerable discoloration and marked brittling of the cellulose so that it fragmented when picked up. Microscopic sections, in which there was approximately grade 2 to 3 disintegration of the cellulose after 3 days were examined at intervals until the 7th day. The persistent portion appeared to be small eosinophilic masses which were irregularly placed throughout the section. All elements of the tissue appeared to disintegrate at the same rate of speed.

Some collected pooled serum and pieces of gauzelike material were placed in a series of tubes and examined at daily intervals. On the 1st day there was slight disintegration and fuzziness of the cellulose and on 4th day disintegration grade 3. By 7th day few fibers were present. The serum was not kept at 37 degrees C. that is at body temperature. Whether this would cause an increase in the dissolution of the gauze has not been determined.

When oxidized cellulose was placed in whole blood there was grade 2 dissolution after the 1st day by the 3d day only an occasional fibril and by 4th and 7th days none. This indicated that dissolution began on about the 2d day and reached a maximum on 7th day. Whether body temperature or incubation would hasten this process has not been determined.

The best fixative appears to be either 95 per cent or absolute alcohol. This fixes the tissue with no further dissolution of the cellulose when the specimen is put into other fixatives.

Cellulose that had been left in wounds for $2\frac{1}{2}$ and $4\frac{1}{2}$ days, respectively also was examined. After $2\frac{1}{2}$ days some small eosinophilic masses, resembling the material previously mentioned remained. There was only slight polymorphonuclear leucocytic reaction and the remaining particles of cellulose were mingled with fibrin erythrocytes, and necrotic

brain substance. At $4\frac{1}{2}$ days, this process had progressed so that no fibers were seen.

CONCLUSIONS

Specially prepared absorbable oxidized cellulose either gauzelike or cottonlike in type, with a solution of thrombin was tried by various surgeons of the Mayo Clinic as an aid to hemostasis in 60 cases. Results were encouraging. Hemostasis was excellent and immediate in 37 cases and satisfactory in 20 cases.

The hemostatic effect of oxidized cellulose seems to depend on its sticky character when saturated with blood. It produces minimum tissue reaction and is relatively nonirritating and readily absorbable. It can be removed from a wound without the secondary bleeding that so frequently occurs after removal of ordinary gauze. Since cellulose is a foreign body however use of a large amount of it in a deep nondrained wound may be unwise.

In pathologic studies the pathologist found no fibers remaining in the tissue $4\frac{1}{2}$ days after the material had been introduced into the wound. The reaction in the tissue was limited to presence of a few polymorphonuclear cells.

The results of this study would seem to justify further clinical trial of absorbable oxidized cellulose both with and without thrombin. In a few recent cases excellent hemostasis has been obtained with cellulose without thrombin. The field of applicability seems wide and uses other than as a hemostatic agent are possible however it should not be substituted for careful surgical technique.

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A CLINICAL APPRAISAL OF CETYLPYRIDINIUM CHLORIDE AS A SKIN ANTISEPTIC

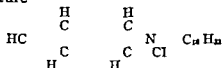
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In *vitro* experiments (2) indicate that solutions of cetylpyridinium chloride have marked germicidal activity. The purpose of this investigation is to study the efficacy of these solutions when used to prepare the skin preoperatively in the surgical clinic. The limitations of skin degerming processes are well known. In presenting this study it is realized that no method or agent or combination of the two in clinical use at the present will consistently sterilize the skin. Clinical methods are quantitative degerming procedures. The organisms have their numbers reduced but cannot be eliminated in 100 per cent of trials.

Because cetylpyridinium chloride is not well known to the clinician its characteristics and properties will be briefly reviewed. In 1916 Jacobs and coworkers (6, 7, 8) pointed out that this group of compounds has strong germicidal properties. More recently Muller and Baker (10) and Harrison and Miller (1) compared the *in vitro* properties of soap and certain cationic detergents. Soaps fall into the group of anionic detergents since in them the alkyl radical carries a negative charge. Cationic detergents are so named because their alkyl radical carries a positive charge. The method of these workers was to study the metabolism of freshly prepared suspensions of micro-organisms in the Warburg manometric apparatus. In their study of 6 gram negative and 6 gram positive organisms they found that the cationic detergent is a more general inhibitor of bacterial metabolism than the anionic. They concluded that while gram positive and gram negative micro-organisms were equally sensitive to the action of cationic detergents, the anionic detergents studied selectively inhibited the metabolism of the gram positive organisms. They state (1) studies of homologous series of straight chain alkyl

sulfates and sulfoacetates (C_8 to C_{14}) demonstrate that maximum inhibition is exerted by the 12, 14 and 16 carbon compound (lauryl, myristyl and cetyl).

Cetylpyridinium chloride, a cationic detergent, is a quaternary ammonium salt having this structure:



It is a white crystalline solid which dissolves readily in water forming an odorless solution slightly alkaline in reaction. It is sometimes called an invert soap, differing from other soaps in containing no metallic base and in being chemically reversed in respect to the electrical charges of the group in the molecule. This product has both hydrophilic and lipophilic properties. The hydrophilic properties originate from the ionic properties of the salt and the lipophilic properties originate from the long chain structure of the cetylpyridinium cation which is attracted to lipoids. When cetylpyridinium chloride is placed in contact with water and lipoids a definite orientation of arrangement establishes contact with both types of matter and is responsible for a high tissue penetrating action. This solution with its wetting and detergent properties has increased power to penetrate pores and minute crevices. The importance of such properties in a skin sterilizing agent need not be emphasized. Dilute solutions of this salt do not precipitate blood serum or egg albumen. By more concentrated solutions the proteins are precipitated but redissolve on addition of more cetylpyridinium chloride. *In vitro* experiments (2) indicate that the presence of serum does not abolish the compound's germicidal activity. The germicidal potency of all quaternary ammonium salts is reduced by soaps. However no other significant incompatibility has been discovered.

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In *in vitro* experiments comparing germicidal activity against *Staphylococcus aureus* cetylpyridinium chloride was shown by Blubaugh, Botts and Gerwe (3) to be superior to all other compounds tested. Blubaugh and coworkers (4) demonstrated too that this germicidal effect is not a selective one but is exerted against all the common pathogens. Further study by Green and Birkeland (5) indicates that cetylpyridinium chloride is an effective germicide for bacterial spores.

Warren, Becker, Marsh, and Shelton (11) have reported the pharmacological and toxicological properties of this compound. The alleged curare like action of toxic doses has been confirmed. In experiments for the study of acute and chronic toxicity it was found that doses many times larger than a patient would ever receive were required to produce untoward effects in the experimental animal. Also no significant irritative effect was found when it was applied to the skin and mucosal surfaces of patients.

METHOD

With the experimental background for the use of cetylpyridinium chloride as a germicide established an attempt at clinical evaluation of this agent was undertaken. It must be strongly emphasized that this study includes numerous possibilities for error in its experimental method. The sterile media and the cultures were transported several miles from laboratory to operating room by untrained personnel. The preparation of each operative site was supervised by one of a group of ten house officers. It is inevitable that there should have been minor variations introduced by individual surgeons. The opening and closing of the culture bottles was done by nurses and operating room aids whose training in bacteriologic technique was more or less deficient. These are but a few significant variants which were not controlled.

In this investigation the pathogenicity of the contaminants was not determined. The microscopic examination showed the morphology to be for the most part large gram positive cocci and rods similar to the non-pathogenic air contaminants frequently encountered in routine culture work.

TECHNIQUE

For *experiment 1* the operative site was shaved in the usual way soap and water lather being used. This preparation was done on the ward the night before operation or in the operating room as the initial step in the preparation. A cotton swab culture (the swab dipped in sterile normal saline solution or distilled water) was taken from the operative field after the simple cleansing of the skin with soap and water alcohol and ether. A second swab culture was taken from the area after application of the tincture of cetylpyridinium chloride. Then by means of the same technique that is used for taking pinch grafts, a small fragment of skin for culture was taken from the center of the painted area. All specimens for culture were placed in beef infusion broth at once and transferred to the incubator. The concentration of skin antiseptic and the volume of broth in the culture container were changed during this experiment.

For *experiment 2* the operative site was shaved as here outlined. A cotton swab culture was taken from the operative field after it had been scrubbed in a rotary pattern, cotton gauze soaked with 1:100 aqueous solution of cetylpyridinium chloride being used. This was done by one of the operator's assistants before he had prepared his own hands and arms by scrubbing. The gauze used was not sterilized. The preceding two details apply also to experiments 3 and 4. Ten minutes were to have been spent in the scrubbing process, though it is probable that in some cases the period was shortened. The gauze sponge was changed for a freshly soaked one four to six times during the scrub of each field. A second swab culture was taken from the same area after the application of the tincture of cetylpyridinium chloride. Then as in experiment 1 a small piece of skin for culture was taken from the center of the prepared area.

For *experiment 3* the patient was shaved on the ward or in the operating room but the usual soap and water lather was replaced by the 1:100 aqueous solution of cetylpyridinium chloride. It was thought that any soap left on the skin after shaving might reduce the effectiveness of the cetylpyridinium chloride used subsequently. Because of the well known

"incompatibility" which had been demonstrated *in vitro* it was proposed to eliminate any such reaction in the clinical application of the germicide. No attempt at special cleansing was made at the time of the shaving. As in experiment 2 the cotton swab culture was taken from the operative field after it had been scrubbed 10 minutes with gauze soaked in 1:100 aqueous cetylpyridinium chloride. The skin fragment was taken from the prepared area as in the other experiments. No tincture was added to the field prepared by this single washing process.

In experiment 4 the preparation of the operative site was further simplified. As in experiment number 3 shaving was done with the 1:100 aqueous cetylpyridinium chloride instead of soap and water lather. However the cotton swab culture was taken from the operative field after that area had been scrubbed only 5 minutes with gauze soaked in 1:100 aqueous cetylpyridinium chloride. The skin fragment was then taken for culture as in all other experiments. The incision was made without further treatment of the field.

All cultures were incubated 7 days at 37 degrees C. Daily observations were made for the growth of contaminants. In experiments 3 and 4 mixed suspensions of *Staphylococcus aureus* and *Escherichia coli* (one 24 hour culture of each) diluted to perceptible cloudiness (approximately one half billion organisms per c.c.) in 0.1 cubic centimeter amounts were added to each bottle which showed no growth. All were incubated at 37 degrees C. All inoculated samples supported growth of the inoculum in 24 hours.

DATA AND OBSERVATIONS

1. *Bacteriologic studies* Experiment 1 may be divided into two parts. In part A the skin was painted with 1:1000 tincture of cetylpyridinium chloride. It was decided to use a more concentrated tincture after 122 cases had been collected. Accordingly in part B the 1:500 tincture was used and the results recorded in the first 122 cases. This group is used because it is comparable with the series in which the 1:1000 tincture was used.

Part C covers 395 cases inclusive of those listed in part B and consists of the total cases

in the series in which the 1:500 tincture was used. It should be explained that there were 411 cases in the original group. In 16 of these it was found that there was a positive culture after the application of tincture though the swab culture taken after simple washing had failed to show any contaminant. Several factors may figure in the explanation of this. The swab may have failed to pick up organisms that were still present and viable after the washing and were picked up after the application of the tincture. The swab may have carried enough soap and water to inhibit the growth of bacteria carried to the 10 cubic centimeters of broth. The same effect may have been lost by the dilution factor when organisms were carried from the painted surface to the 150 cubic centimeters of broth. Or these may be cases in which there was contamination from the outside after the application of the tincture. It is apparent that these cases of negative culture after the wash but positive culture after the application of tincture should be eliminated from any series which attempts to evaluate the clinical germicidal value of the tincture.

A comparison of results of part A with part B suggests several points. In this particular study washing the skin with soap and water, alcohol and ether was not very effective as determined by the swab culture method. There were positive cultures in 78.7 per cent of the cases of the first series and 86.1 per cent of cases of the second. Lee and Hoxworth found contamination in only 22.6 per cent of their series of 216 cases. It should be noted that careful standardization of the technique of the soap and water, alcohol and ether wash was not done. This step in the procedure was regarded as a preliminary to the application of the skin antiseptic and such important factors as length of time of scrubbing were not regulated. It is certain however that our procedure was comparable with that of Lee and Hoxworth. So it may be said that such a preliminary skin preparation with soap and water, alcohol and ether may vary widely in effectiveness (22.6% to 86.1% positive cultures) measured by swab culture.

Further comparison of results in parts A and B shows that the concentrated tincture

may not have been more germicidal than the dilute as estimated by swab cultures in the 2 groups of cases (51.3% in part B and 55.7% in part A). Cultures of the skin fragments suggest that in the deeper levels of the skin the 1:500 tincture may have exerted a greater germicidal effect than the 1:1000 tincture (37.7% in part B and 58.2% in part A). It should be pointed out however that the formation of conclusions from a study of groups of this size may not be justified. This point becomes obvious on comparison of part B with part C. The methods applied to those two groups were identical. Part B was formed of the first 122 cases. Part C included part B and 273 more cases. The differences that exist between parts B and C are the variations found in comparing a group of 122 with a second group of 395 of exactly the same cases. It is plain that groups of 122 may not form bases from which to draw detailed conclusions.

Finally, consideration of the frequency of positive cultures—27.6 per cent in the skin fragments, brings out the conclusion that this method of preliminary scrubbing with soap and water and application of tincture of cetylpyridinium chloride is not very effective against organisms in the deeper layers of the skin.

Experiment 1 is considered in two parts before considering it as a whole. In part A the swab culture obtained after the application of cetylpyridinium chloride wash was placed in a tube containing 10 cubic centimeters of broth. In part B the swab obtained after the wash was placed in a bottle containing 150 cubic centimeters of broth. This change in experiment plan was made to reduce the effect of the trace of cetylpyridinium chloride solution which must be carried by the swab from the washed surface to the culture media.

Comparison of part A with part B of experiment 2 shows that in part A cultures taken after the initial cetylpyridinium chloride wash there were contaminants in 4.1 per cent of cases while in part B there were contaminants in 9.9 per cent of cases. Before concluding that this difference in number of positive cultures came as a result of dilution of the germicide carried into the media by the swab it should be noted that on comparison of positive

cultures found after application of the tincture and in the skin fragments there is a difference of equal magnitude between parts A and B. Since there was no alteration in the experiment plan related to these two groups of cultures, it suggests that all the differences in percentage of positive cultures may have come from the same cause and that the introduction of a dilution factor failed to disclose a definite bacteriostatic effect by the cetylpyridinium chloride carried to the culture media.

In part C of experiment 2 several points are obvious. If the swab culture method can be relied upon to give a sample of surface flora, the simple method of scrubbing with the solution of cetylpyridinium chloride is an effective method for killing bacteria on the skin's surface. After this wash there were positive cultures in 6.3 per cent of the cases. The application of the tincture did not definitely augment the bactericidal process. There were contaminants then in 5.9 per cent of the cases.

The most striking results were found on culture of the skin fragments. Here positive cultures were found in only 3 per cent of the cases. The reason for the smaller number of positive cultures from the fragments than from the skin surface is not clear. Organic matter on the skin at the time of the washing may inhibit the activity of the agent and so allow growth of organisms in swab cultures. The swab cultures of the surface covered a large area many times greater than the surface area of the skin fragment. The fragment may have carried with it to the media enough of the agent to effect some degree of bacteriostasis. Tissue fluid from the bit of skin may have acted with the cetylpyridinium chloride in a synergistic way.

In experiment 3 the skin of 257 patients was shaved, 1:100 aqueous cetylpyridinium chloride being used. Cultures were taken from swab and skin fragment after a 10 minute scrub with the same aqueous solution. The swab culture was positive in 15.6 per cent of the cases. Five and four tenths per cent of the skin fragments cultured showed contamination. In detailing the technique it was suggested that because soap is known to reduce the germicidal activity of cetylpyridinium chloride *in vitro* the bactericidal effect of this

agent might be increased by eliminating all traces of soap from the area being prepared. In experiment 2 the skin of 271 patients was shaved with soap and water and cultured by swab after a 10 minute scrub with 1:100 aqueous solution of cetylpyridinium chloride. Five and nine tenths per cent of the swab cultures showed contamination. In this third experiment where no trace of soap could have been on the skin 15.6 per cent of the swab cultures showed contamination. It would seem that any trace of soap left on the skin after the usual shave did not have a significant effect upon the germicidal activity of the aqueous solution of the cetylpyridinium chloride. Only the swab culture results are compared because the skin fragment results are not comparable. In experiment 2 1:100 tincture of cetylpyridinium chloride was added to the skin before the fragment was cut.

In the fourth experiment the skin of 232 patients was shaved 1:100 aqueous cetylpyridinium chloride being used. Cultures were taken by swab and skin fragment methods after a 5 minute scrub with the same aqueous solution. The swab culture showed 13.8 per cent of the cases to be contaminated. Ten and three tenths per cent of the skin fragments cultured showed contamination. This latter finding may indicate that the germicidal effect obtained by the 10 minute scrub is greater than that obtained in 5 minutes of scrubbing (5.4 per cent positive cultures compared with 10.3 per cent). Change of the scrubbing time from 10 to 5 minutes made no significant difference in results obtained by swab culture (15.6 per cent positive cultures compared with 13.8 per cent).

As described in the technique mixed suspensions of *Staphylococcus aureus* and *Escherichia coli* in 0.1 cubic centimeter amounts were added to each bottle which showed no growth in experiments 3 and 4. All bottles supported growth of the inoculum in 4 hours. That this finding is of some significance is suggested by the report of Lee and Helmsworth. They concluded that the apparent high degree of effectiveness of ethylmercurithiosalicylate (merthiolate) indicated in their swab culture study was probably due to the bacteriostatic effect of that agent carried on the swab into

the culture media. Because all negative cultures in experiments 3 and 4 supported growth of the inoculum it appears that such a misleading bacteriostatic effect was not present in this study.

2 *Physical characteristics* All dilutions of the tincture are now tinted with a special reagent dye. In all alkaline medium as in the presence of traces of soap it changes from its red-orange color to a yellow orange. This warns of the incompatibility which has already been mentioned. It coats the skin surface smoothly and its color sharply demarcates the prepared area.

The aqueous solution of cetylpyridinium chloride being colorless odorless and practically tasteless is easily used as a germicide. When used in the scrubbing process it forms a fine colorless foam not unlike that of white soap and water.

3 *Delayed and secondary effects* In one case in the entire group there was local vesiculation and erythema suggesting an allergic reaction. While experiment 4 was being conducted a small number of patients were found to have vesicles beneath the adhesive tape at the periphery of the operative site. The cause of this reaction may include several factors. It was found only when the adhesive was in direct contact with the skin. Change in adhesive tape has been apparent to all users in the past year. The skin had been coated with tincture of benzoin before the application of the tape. The composition of the tincture of benzoin may have been altered during the past year. The patients showing the reaction were often those who had lain 1 to 3 hours on linen soaked in 1:100 aqueous solution of cetylpyridinium chloride. The reaction may have resulted from overlong contact with the germicide.

The reactions mentioned were not of a nature to limit in any way the use of the 1:100 aqueous solution of cetylpyridinium chloride.

4 *Applicability of method* Before this study at the Cincinnati General Hospital the operative field in all cases was first cleaned in the operating room with soap and water, alcohol and ether. The technique of experiment did not include this step. It was replaced by the simpler method of scrubbing

with the germicidal solution. In experiment 3 the procedure was further simplified. The application of the tincture to the operative site was eliminated. Experiment 4 employed a method equally simple with the additional advantage of reduction in time required for preparation of the operative site. It is our opinion that methods employing the fewest agents and requiring less time will be most efficiently carried out by operating room personnel. The conservation of time will be a detail of some importance to the surgeon.

5 *Economy* A study was made of the cost incurred by using 1:100 aqueous solution of cetylpyridinium chloride as the sole agent in preparing an operative field. A contrast study was made of the cost with soap water alcohol, ether and various tinctures. The cost of the former method was much less than half that of the latter.

SUMMARY

1 The physical characteristics, the bactericidal properties *in vitro* and the pharmacological and toxicological properties of the germicidal agent cetylpyridinium chloride have been reviewed.

2 A clinical study of the germicidal activity of two dilutions of a tincture of cetylpyridinium chloride has been presented.

3 A clinical study of bactericidal effect has been presented in which the operative site was scrubbed 10 minutes with an aqueous solution of cetylpyridinium chloride and then painted with a tincture of cetylpyridinium chloride.

4 A clinical study of bactericidal effect has been presented in which the operative site was scrubbed with 1:100 aqueous solution of cetylpyridinium chloride in one experiment 10 minutes and in another 5. No further treatment was given the site in this group of cases.

CONCLUSIONS

1 The preliminary preoperative skin preparation with soap and water alcohol, and ether may not be an efficient germicidal process if all details of the procedure are not carefully controlled.

2 Tincture of cetylpyridinium chloride applied to operative fields washed with soap and water alcohol, and ether has a definite germicidal effect.

3 Scrubbing operative fields with a 1:100 aqueous solution of cetylpyridinium chloride produced a striking germicidal effect.

4 Aqueous solution of cetylpyridinium chloride is well tolerated by the skin of patients. Its physical characteristics make it acceptable to operators and its use is economical.

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TREATMENT OF POSTOPERATIVE INFECTIONS FOLLOWING INTERNAL FIXATION FOR FRACTURE OF THE NECK OF THE FEMUR

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THE frequency and gravity of postoperative infections following internal fixation for fracture of the neck of the femur are not appreciated because many instances are concealed and few are reported. In a recent well ordered article Siris and associate reporting 157 instances of fracture of the neck of the femur cited 53 operations for internal fixation 47 with the Smith Petersen nail 5 with this nail plus the Hawley bar 1 by Moore's pins 1 by external fixation with the Roger Anderson apparatus (which became infected) and 3 by Russell traction. The total mortality was 5 equalling 9.6 per cent. Six instances of external pin insertions one intracapsular and 5 extracapsular fractures of the femur (intertrochanteric?) after operation developed infection at the site of pin insertions 5 died and the authors say:

If other surgeons have experienced the same disastrous consequences we have not found any mention of it in the literature. Neither have I. Yet I have been seeing and struggling with these calamities for several years.

I wish to confine my report to the title given namely postoperative infection following clean elective internal fixation for fracture of the neck of the femur assuming that the operation has been faithfully and properly performed by a competent surgeon and not by a casual operator. Also that the operation was performed in a hospital operating room under the usual aseptic conditions for such procedure that proper (and hopefully a three series program) roentgenologic control has been used in the fixation and that the postoperative care of the wound and patient has been standard and adequate.

Some of these operative wounds will become infected even as a certain percentage of all

clean elective operations still plague us with infection notwithstanding our best efforts at prevention and the rapidity and skill with which operation is performed. The early and local infection and osteomyelitis in the neck of the femur set up after internal fixation may not be caused by any definite local lowered resistance of the bone. It may be attributed to local thrombosis following the fracture of the bone to which is added the additional trauma of the inserted foreign body. The local trauma set up by the fixation agent alone in an old fracture with long since subsided and absorbed hematoma of the acute bone severance may be enough to cause local thrombosis and possibly necrosis. This may be aggravated by prolonged or unskillful insertion of guide wires and fixation agents or their several times repeated withdrawal and reinsertion to correct positions. Naturally any blood stream infection may lodge in this area for settlement and growth or the slightest amount of inborne infection on fixation nail skin or tissues of patient or usual sources from gloves and respiratory systems of the operators, hematoma formation or poor skin closure may start the affair. It does happen.

These patients come to the consulting surgeon or into the services of charity hospitals generally late from 3 to 12 months after occurrence of infection. The onset is usually insidious and not alarming. Failure of recognition of the magnitude of the situation is not uncommon. Attempts at renailling if nails have slipped or distraction of fracture surfaces has occurred may unhappily be made. But usually the fixation agent is finally withdrawn by the primary operator or a colleague and little else is done. The patient drifts into a condition of chronic osteomyelitis with bed confinement is almost always without fixation in plaster splints, and the surgeon hoping for a miracle may give doses of sulfa drugs or

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Read before the Western Surgical Association, Chicago, December 9-14

penicillin or both. Loss of weight and strength ensue discharging sinuses appear at the hip death of the head of the femur may be realized and pathological dislocation at the hip finally discovered. The patient may proceed to death from this exhaustive sepsis because in some instances the sepsis involves the acetabulum the ilium and the trochanteric portion if not the shaft of the femur. Decubitus ulcers are almost always found. The head of the femur although dead or lying in the infected area may unite with the neck of the femur if the internal fixation job has been well carried out.

As a result of the sepsis and frequent lack of external splinting dislocation at the septic hip may occur before or after the internal fixation agent is removed. The head of the femur may retain its fixed relationship with the neck even if united only in part. Such a head on removal is found to be eroded and necrosed, not so much on cartilaginous and joint surface as on posterior aspect, possibly on account of a gravity pool of pus forming posteriorly as patient lies in bed or spilt.

If the infection in the track of the fixation agent and the hip joint is recognized early the use of sulfa drugs or penicillin with immobilization may control it before local bone death and free pus formation occur. I have never yet seen such an instance. If free pus and abscess form chemotherapy will be effective only when accompanied by free and yet nondestructive drainage of the hip joint area, along with the removal of the fixation agent and dead bone followed by the application of a wick drain with vaseline gauze and long continued immobilization. Patients who are desperately depressed from the sepsis and malnutrition require long preparation with blood transfusions and hyperalimentation before operation for extensive drainage manipulative proceedings or sequestrectomy is possible. Skeletal traction on the leg is of great assistance in these operations to aid in the manipulative procedure and for postoperative sure fixation in the chosen position of traction and abduction of the leg. Operations for primary bone shelf support above the acetabulum nail screw or bone transplant fixation to the pelvis osteotomy or arthro-

plasty do not seem wise in the presence of the extensive gross infection about the hips.

In young patients, when infection has subsided for many months secondary operations may be indicated for great looseness of the hip pain on weight bearing or embarrassing shortening of the leg after use. Such a late operation may be desirable to give better functional and cosmetic results. A final movable hip may be better for some patients than a solid bony ankylosis. In most instances healing with a flexed or abnormally angled hip can be bettered by osteotomy and restoration of better weight bearing axis. The treatment may be summarized as follows:

1. Recognize infection identify organism.
2. Prepare patient for operation.
3. Insert Steinmann pin through tibia or heel withdraw fixation agent in hip remove head of femur (do not cut off greater trochanter) replace neck in acetabulum apply narrow vaseline gauze drain and administer sulfa drug locally.
4. Close most of wound apply body plaster with leg in slight abduction.
5. Start penicillin 100,000 units first 24 hours intravenously 10,000 units every 4 hours thereafter.
6. Leave immobilized until sinus is healed and bony union attained if possible.
7. Operate later for reconstruction of hip if needed.

CASE 1: G. M. male, aged 54 years on April 6 1938 had a fracture of the neck of the left femur. Three steel pins were inserted after good reduction shown in the posteroanterior roentgenogram, April 7 1938 no lateral roentgenogram was taken. Wound infection followed. By August 5 1938 the pins had been removed the head of the femur was now rotated and in valgus position because there had been traction on the leg and no union at the neck. By August 31, 1938 this condition was enhanced and the rotated head of the femur had come completely out of the acetabulum. In September 1938, the head showed increased density irregularity and spotty absorption—dead. The upper margin of the acetabulum began to melt away and there appeared a doubtful extension of the osteitis to the trochanteric portion of the femur and down the shaft where there were areas of potty absorption and new bone formation beneath the periosteum. Pus (staphylococcus) drained freely from hip. Thigh was soggy fluctuant. Temperature reached 100 degrees daily and there was great loss of weight and strength.

The diagnosis when first seen by me on September 30, 1938, was ununited fracture of the neck of the femur with dead head infected gross infection of the left hip joint with dissolution of the acetabular margins and pathologic dislocation of the hip osteomyelitis of the femur and ilium. He was next seen on November 8, 1938. A few attempts to get him to sit up in bed or on a chair had resulted in immediate rise of temperature. The left thigh was now enormously swollen and tender numbness developed in the left foot, the dorsalis pedis artery was palpable, free pus discharge issued from the hip. His general appearance had deteriorated appetite became poor the tongue was red glazed and dry and he had lost weight. On November 14, 1938 he was transferred to my services at the Presbyterian Hospital. After the use of hot applications and bed rest the left leg being supported in a Thomas splint with fixed traction from skin to splint he was rendered afebrile and by the last of November, 1938 he was able to be out of bed. A walking caliper was fitted to him and the necessity of hip joint disarticulation began to fade. He was given supralimentation and encouraged to be up all he could. About February 17, 1939 temperature again rose and considerable swelling at ankle and edema in left thigh developed.

On February 24, 1939, an operation was performed to insert skeletal traction in the left heel. An x-ray examination later showed that the femur was being pulled down and the head lay just above the upper edge of the acetabulum. Later a forceps passed into the hip sinus struck rough bare bone of the trochanteric region and then passed easily on up toward head of femur but one could not tell exact source of purulent discharge. Fever still present.

On March 8, 1939 an operation on the hip was performed. After fixation on the fracture table taking advantage of the Steinmann pin through the calcaneus for this purpose we excised the sinus opening in the left hip by an elliptical incision 8 inches long. Pus ran out freely. The greater trochanter of the femur was cut off obliquely with a wide chisel and with muscles attached retracted back out of the way. The left leg was rotated outward and the head of the femur visualized pus pockets were found about it. The head seemed attached in fair position by bony union to the trochanteric portion of the bone. Believing that there was deeper infection involving the ilium and acetabulum the head of the femur was then cut off just below the level of the original fracture. When the head was thus removed it was found that its posterior half was necrotic, greatly eroded and covered with pyogenic granulations. The acetabular cavity could then be palpated and seen. One loose eroded piece of bone 3 centimeters long was found on the antero-inferior border lying free in pus and granulations. This probably represented a fracture of the acetabulum not clearly seen in any roentgenogram. All this cavity and granulated area was then gently curetted. By tightening the traction on the long axis of the leg along with some inversion and abduction the

cut-off neck of the femur was inserted into the bony pocket of the ilium. The tissues were partly sutured around the upper portion of the femur. One vaseline gauze pack was laid down the axis of the neck of the femur and the main portion of the wound was approximated by through-and-through silk worm gut button sutures the drain being left protruding. A plaster-of-paris encasement was applied extending from the base of the left toes including the whole left leg and pelvis to costal margin and extending down the right leg to the knee.

By March 28, 1939 the final end of the vaseline gauze was withdrawn. Still some purulent drainage was noted. Temperature was normal. April 28, 1939 the nail through the left heel was withdrawn but the plaster was not disturbed. There was less drainage from the hip wound. On May 1, 1939 raw bone could no longer be felt at depth of hip sinus when sterile forceps was inserted. On May 21, 1939 he was removed from body plaster and the roentgenogram showed that cut-off neck of femur was still apposed to old curetted acetabulum but amount of attempted bony union there could not be certified.

He gradually went on to ambulation via a wheel chair all discharge from the hip ceased. He was continued on sulfanilamide until August 15, 1939. About this time there was shortening of the leg slight inversion good pulsation in the dorsalis pedis 30 degrees motion in the knee joint and he was walking wearing a caliper support. An x-ray film showed considerable spotty absorption in the left femur but no definite areas of osteitis. He left the hospital August 22, 1939 with 2 inches shortening of the left leg walking on a caliper with crutches able to get out of wheel chair and into bed alone.

At an examination on July 20, 1940 his leg was 1 1/2 inches short. He walked without support, presented great muscular atrophy around the left hip no real bony fusion the knee joint motion 90 degrees. He expected to return to work on January 1, 1941.

Final examination on October 20, 1944. He walked with a slight lump in the left leg wearing an elevation of 1 1/2 inches under the left heel only. He can flex the left thigh 30 degrees has a few degrees of abduction stands perfectly erect and can cross the left leg over the right. A roentgenogram at this time shows the cut-off neck of the femur quite well inserted in the old acetabular area with a well developed bony shelf at the upper margin assuring proper support and weight bearing with a fair joint space between the head of the femur and acetabulum. The old spotty atrophy in the femur has disappeared. The recovery and reconstruction of the hip area is most satisfactory. He was advised to wear an elevation under the whole left shoe to help balance leg shortening which now equals 2 inches.

CASE 2. A M. male aged 46 years was injured in Texas on January 31, 1913 sustaining a fracture of both rami of the right ischium inferior rami of the left ischium ala of the right ilium near the sacroiliac joint and of the neck of the right femur. He was put in a Jones well leg splint. The fracture of the

neck of the femur was apparently overlooked and finally recognized on April 9, 1943 with overriding and varus deformity with rotation of the head then present. On April 27 1943 the fracture of the neck of the femur was reduced and held by a Lorenzo screw. In a few days as no splint was used he was allowed to walk, and shortly after came to Chicago where he was first examined by me on May 17 1943.

A roentgenogram on this date showed an incomplete coaptation of the neck of the femur screw still *in situ* but the lateral roentgenogram of the hip showed that the head was rotated and angled considerably (30 degrees) although penetrated by the screw. The pelvic fractures seemed to have progressed to a satisfactory healing. On the scar of the recent operation there was a small red area but the patient had no fever no discharge no signs of gross infection. He was put to bed and hot wet dressings were applied to the hip. His white blood count was 7,400 to 8,500. After a week, all redness and evidence of inflammation being gone operation was attempted. The fractured leg measured 1 inch shorter than the opposite leg part of which may have been caused by the bending of the fractured pelvis.

On May 25, 1943 a modified Smith Petersen incision was made, the scar of the first operation being excised to expose the neck and trochanter of the femur. The screw was withdrawn and cultured. A manipulation to obtain a better reduction of the head and neck was performed and the position as seen in the roentgenogram made as he lay fixed on the fracture table appeared quite satisfactory in both anteroposterior and lateral roentgenograms. After a position of satisfactory reduction as shown by x ray the patient was fastened onto the Hawley table with legs in moderate abduction. A new hole was then driven into the head of the femur via the old channel of the screw in the trochanteric area, a bone transplant of suitable size and length obtained from the tibia was inserted after the position of the head and neck of the femur had first been fixed by a Moore nail inserted above the path of the reamer. The wound was closed and a plaster-of-paris encasement was applied. During this operation the patient was given 500 cubic centimeters of whole blood, and a similar amount was given starting immediately after return to bed. On May 27 1943 patient's temperature rose to 101 degrees, and although the wound was not inspected he was put on conventional doses of sulfathiazole. Chest was normal.

On June 4, 1943 the plaster dressing was cut and the skin stitches were removed. There was some bulging of the wound the edges of which separated and bloody pus was evacuated. Five days later his temperature was normal and it was hoped the infection was relatively superficial and under control. It did not prove to be. The wound was later opened further the surface well dressed with sulfathiazole, and a vaseline gauze pack was inserted. By July 7 1943, the discharge had become odoriferous the packing and sulfathiazole were repeated. X-ray still failed to show any definite evidence of infection

in head of femur or hip joint, but fever and pain continued despite gentle handling in plaster dressing. Packing and sulfathiazole at long intervals were replaced, odor and fever and amount of discharge diminished rapidly. No penicillin obtainable.

By August 17 1943 the cast was found to be broken across the groin, permitting some movement of the right leg. The plaster had to be removed. A new x-ray examination showed to our sorrow that the head of the femur was greatly rotated, but with bone graft and pin still *in situ*. I believe this rotation occurred when I had unhappily chosen the old screw path for insertion of reamer by means of which I hoped to make a new path into head fragment.

The plaster was changed and the position not disturbed nor was the bone transplant broken, the foot and leg remaining in well corrected position. He was removed from the second plaster on September 16, 1943 with only a small fistula in the right hip, measured by probe only 1 inch deep. He was allowed a wheel chair and later crutches for ambulation with out bearing weight on that right leg. Two weeks later he developed a diffuse cellulitis about the wound in the right hip which yielded to hot dressings and continued sulfa drugs until he was restored to normal temperature and finally sent home on October 23 1943 walking with the help of crutches.

When seen a month later he had some discharge of pus from the sinus in the right hip pain in the joint, and inability to raise his leg from the table. On December 2 1943 an abscess around the hip wound was drained no loose or dead bone deep in the hip region was palpated the sinus walls were excised or curetted, sulfathiazole was implanted, and a vaseline pack inserted. A new plaster-of-paris immobilization was applied 6 days later. By December 15 1943, his temperature was subnormal, his pain gone. X-ray pictures taken at this time failed to prove necrosis of the head of the bone the pin and transplant were still holding.

A few tenths of a degree of temperature and some discharge from the hip persisted. X-ray examination with the help of planigraphs on January 31 1943 showed quite certain evidence of death of the head of the femur although still fixed in the position obtained at operation.

Consequently on February 7 1944, the old wound was reopened on the right hip and the Moore pin and the head of the femur removed after it had been split with a chisel because it was so firmly imbedded and adherent in the acetabulum. The bone transplant in the trochanteric portion of the femur was not disturbed. The hip joint area was gently curetted and wiped out. The leg was again put in a functional position and the wound was partly closed, a vaseline gauze pack being left in its depth. Body plaster was applied. Whole blood transfusion of 500 cubic centimeters was given during operation.

By February 1944 his temperature was normal. The sulfathiazole was discontinued 4 days later. The cast was cut open for dressing on February 11 1944 and a large amount of foul smelling

discharge was disclosed. The button sutures were removed and a new vaseline gauze pack was inserted. He was still fever free. This was repeated on March 1, 1944, with saturated dressings found but no fever and a smaller pack was inserted. At this time he was given a total of one million units of penicillin in consecutive doses of 10,000 units every 4 hours. On March 15, 1944, he was removed from the plaster when there was very slight discharge. He had no fever. Temperature was normal. On April 26, 1944, he went home. The sinus was practically closed. The sinus has remained closed, and he walks on crutches.

At a later examination on August 28, 1944, he could walk on crutches several blocks. He wore a support under the right foot to compensate for the shortening of that leg. The sinus was completely closed and healed. An x-ray examination showed no dead bone or sequestra and a doubtful bridge of bone union between the trochanteric fragment of the femur and old acetabulum. There was no change in the axis of femur. The foot was in excellent weight bearing position with no additional shortening.

This patient's real infection was first noted on June 4, 1943. Ten months later on April 1, 1944, penicillin was started 100,000 units being given by continuous intravenous drip the first 24 hours followed by 30,000 to 80,000 units intramuscularly daily thereafter until he had been given one million units.

During the course of his earlier treatment he seemed to develop an outward reaction to sulfathiazole which was given in maximal therapeutic dosage from February 5 to February 7, 1944, February 10 to February 14, 1944, and March 14 to March 30, 1944, which apparently caused a secondary rise in temperature, some cyanosis and interference with his appetite. We concluded that the final closure of this difficult sinus was probably due to 3 factors: the drainage with removal of dead bone, the use of penicillin and the immobilization, probably the least important of the three.

CASE 3. H.D., female, aged 54 years, fell in a distant eastern city and broke the neck of her right femur on November 29, 1943. She was taken to a hospital and a Smith-Petersen nail was inserted December 1, 1943. The films made on the operating table showed an apparent good reduction. There was an almost immediate postoperative temperature of 104 degrees and 7 days after the hip operation a probe inserted into the wound led to the evacuation of 2 ounces of old blood with a suspicious odor as described by her surgeon. This on culture was green? *Staphylococcus aureus*. Two days after operation she was suffering from infection of the throat and soft palate

and a yellowish membranous deposit thereon. A portable roentgenogram this same day showed early patchy bronchopneumonia in both lungs. Sulfadiazine was administered. A roentgenogram on December 29, 1943, showed that the Smith-Petersen nail did not project into the head of the femur but lay on the upper anterior surface of the head fragment with angulation (coxa vara) of the head and neck of the femur and no opposition between the fracture surfaces. After consultation it was decided to remove the pin and apply a plaster-of-paris spica to the hip. This was done on January 10, 1944, enclosing the entire right leg and the left leg to the knee. In March, 1944, the patient was given 2 courses each of 1,000,000 units of penicillin. Her fever subsided late in January except for one recrudescence up to 102 degrees on February 2, 1944. The plaster-of-paris dressing was removed April 28, 1944, and the patient was allowed to move the limb to sit up in bed and was found to have a right foot drop, supposedly caused by pressure of the original plaster dressing. The sinus in the right hip still continued discharging serosanguineous material.

She entered the Presbyterian Hospital, Chicago, June 5, 1944, able to walk on crutches with a discharging sinus on the right hip, a shortening of the right leg of 2 1/2 inches, paralysis of the right peroneal nerve, severe pain and stiffness in the left arm and hand, white blood count of 6,300 to 7,500. The last complaint she believes has followed attempts to lift herself by a sling to an overhead bar while in plaster-of-paris. A roentgenogram of this date shows a partially dissolved and dead head of the right femur, spotty atrophy in the trochanteric portion of the femur and ilium and an upward displacement of the femur accounting for the shortening mentioned. A splint was made to support the right drop foot.

Her general condition was very good and an operation was decided on for June 6, 1944. A Steinmann pin was inserted through the right calcaneus and she was fixed onto a Hawley table. The scar of the previous operation on the right hip was completely excised. The hip joint area exposed by deep dissection without cutting off the greater trochanter of the femur and the head of that bone was found quite frozen in the acetabulum (verified by portable roentgenogram). All head fragments and the infected acetabular area were curetted out, the base of the neck was pared down and the leg was then drawn down by traction to as near the acetabular level as possible and abducted about 15 degrees. About 6 grams of sulfathiazole was scattered over the wound surface, which was partly sutured and a loose vaseline gauze drain was left extending to its depth. A body plaster-of-paris encasement enclosing the nail in the right heel and extending down to the left knee was applied. During the operation the patient received 500 cubic centimeters of whole blood. She received one million units of penicillin 100,000 on the first day of operation and about 80,000 each subsequent day. By July 25, 1944, the sinus and wound had completely and lastingly healed. On

August 31 1944 the plaster encasement was removed. A roentgenogram showed no bony union between the trochanteric portion of the femur and the ilium but there was no pain on motion of the hip. The foot drop was improved but there was a considerable area of anesthesia over the dorsolateral surface of the foot. She progressed slowly. By the middle of September 1944, she was able to walk on crutches with additional sole and heel under the right shoe and a spring support for the foot. There was no pain in the hip but considerable distress in the left hip and knee from weight bearing efforts. She left the Presbyterian Hospital October 20 1944, walking partly without crutches, able to go up and down stairs and sit and rise alone from a chair. Numbness and drop of the right foot still persist. She expects to return to work, at least part time in December 1944.

CASE 4. J. D. male, aged 55 years, was injured December 3 1943 when bumped into while ice skating with resulting fall and fracture of the neck of the left femur. He lay in bed 10 days with skin traction on the left leg and then submitted to an operation which he said took 3 hours, 45 minutes. The neck of the femur was pinned with a modified Smith-Petersen nail no plaster dressing or external splint was applied. A few days later when he put his hand down near the wound he encountered a discharge of pus after which some tissue came out leaving an infected wound. He remained in the hospital 3 months during which period he lost 35 pounds in weight and was then sent home in an inadequate plaster dressing with an open infected wound of the left hip which had been dressed daily.

When admitted to the Presbyterian Hospital on May 23 1944 he was in an extremely emaciated condition hemoglobin 8.4 grams red blood count 3,000,000. He lay in bed with the left thigh slightly flexed and adducted with a discharging sinus 4 inches below the greater trochanter of the femur. He also had an indolent pressure sore 2 1/2 inches in diameter over the sacrum the skin edge of which was undermined and overhanging the bone surface forming the base. A similar smaller pressure sore existed over the head of the left fibula. An x ray film showed a spotty absorptive process involving the left ilium and upper portion of the left femur. The fracture of the neck of the femur was ununited. The internal fixation agent had been removed, the head of the femur was necrotic and apparently septic absorption of part of the head and the neck had occurred.

The first step had to be an attempt to raise his general physical condition by the use of whole blood transfusions, vitamins, and liver extract along with as much hyperalimentation as could be forced to get him in condition for surgical operation. These efforts were pursued from May 23 1944 to July 25 1944. He received four whole blood transfusions of 500 cubic centimeters each during this period. Food forcing often caused diarrhoea. His hemoglobin eventually reached 14 grams.

Operation was performed July 25, 1944. A Steinmann pin was inserted through the left heel for control of the leg, the hip was exposed through heavy scar tissue and much soft infected granulation tissue rolled out of the wound. The dead and eroded head of the femur free and easily removable, was evacuated from the hip joint. It was surrounded by bleeding granulation tissue which after curettage led to an almost uncontrollable hemorrhage on the table finally stopped by hot packs. The leg was then drawn down by traction and slightly inverted. The ilium and acetabulum seemed to be the seat of quite extensive osteitis. The wound was partly sutured, 5 grams of sulfathiazole was placed in it along with a narrow vaseline gauze drain. A body plaster-of-paris cast was applied over whole left leg and down to right knee. He was given a blood transfusion on table and immediately afterward, totalling 1000 cc.

By August 14, 1944 he still had a little fever. The gauze pack was withdrawn a large amount of thick pus was evacuated. A small vaseline gauze drain was reinserted. The next day there was a great amount of pus drainage, and it was feared that hip disarticulation alone might save his life. Within 3 days the drainage lessened and in 1 week his temperature became normal.

By September 1 1944, there was practically no discharge and the wound seemed healed. On September 28 1944 however much pus was again evacuated so that the cast had to be removed and local drainage established. This procedure showed a superficial abscess pointing toward the left buttock, which was drained. The exploring finger could not feel any uncovered bone or necrotic pieces. The hip joint area seemed covered by soft and formed granulations so that no ilium or old acetabulum could be felt. A roentgenogram made as he lay on the table at this time showed no necrotic bone but there was a compaction between the trochanteric portion of the femur and the ilium both of which appeared in better health with loss of spotty atrophy. It could not be determined from the roentgenogram that there was bony union between these two surfaces thus immobilized in the presence of infection for over 3 months. Gentle manipulation of the leg, made necessary by the drainage operation seemed to show that there was motion present in the hip region between the leg and pelvis. On account of his extreme emaciation and his complaint of cast pressure, although he had no pressure ulcers, we did not reapply a plaster dressing. Since operation his temperature has remained normal amount of drainage has lessened 2 sinuses are present and packed with vaselin gauze but we still hope for a healing closure and final return to health with stiffened hip. He has now had a total of 39,000 nits of penicillin.

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HYDRONEPHROSIS

Classification and Plastic Repair of Ureteropelvic Obstructions

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A SURVEY of the literature on hydronephrosis reveals the fact that today as a result of the vast experimental and clinical research we possess a more accurate knowledge of the mechanism of hydronephrosis and a far better appreciation of the remarkable reparative power of the kidney subsequent to release of obstruction.

Hydronephrosis follows persistent obstruction at any point in the urinary tract from the urethral meatus to the level of the renal pelvis. One of the most common sites of obstruction is the ureteropelvic junction. Because of certain controversial points it is important to review this phase of the subject and particularly to evaluate the numerous plastic procedures for correction of hydronephrosis based on a classification of ureteropelvic obstructions.

HISTORICAL NOTE

Trendelenburg is given credit for the first attempt at plastic repair of hydronephrosis in 1886 the outcome in his case was unsuccessful—the patient died from intestinal obstruction. In 1892 Kuester reported the first successful plastic operation on the renal pelvis. His operation consisted in reimplantation of the sectioned ureter into the pelvis at its most dependent portion. At approximately the same time Fenger in a clinical lecture described a plastic procedure which he had done for the relief of hydronephrosis due to valve formation and stricture of the ureter at the ureteropelvic junction. Fenger's method consisted of a longitudinal incision at the point of obstruction with transverse closure, an adaptation of the Heineke-Mikulicz principle used in intestinal surgery. Study of the many types of plastic procedures subsequently applied to the correction of ureteropelvic obstruction shows for the most part a close parallelism to methods that have become more or less standard in gastrointestinal surgery. The stimulus of this early work led to an era in which the

renal pelvis became the recipient of surgical attention that was perhaps more enthusiastic than discriminating. There were many failures and even those cases in which the results were termed successful must be accepted with reservation since they antedated the development of urography with its present day precision in the evaluation of surgical end results. Even currently no one is justified in citing an end result as successful without urographic evidence after a sufficient postoperative period. Silent destruction of the kidney may occur postoperatively and give a false impression of cure unless checked by careful urologic investigation.

That the earlier enthusiasm for conservative plastic surgery waned is apparent from a review of the discussion of hydronephrosis at the German Urological Congress in 1921 where the fact was disclosed that up to that time nephrectomy was the generally accepted treatment of hydronephrosis. Since then there has been a gradual recrudescence of interest in conservative plastic surgery which received a real impetus in the symposium on hydronephrosis participated in by von Lichtenberg, Walters, Quinby and others at the annual meeting of the American Medical Association in 1929. Reference to the symposium on hydronephrosis of the American Urological Association at Minneapolis in 1937 furnishes a good cross section of the progress that has been made and other noteworthy contributions in the past few years have served to establish plastic surgery of ureteropelvic obstructions on a firm foundation.

CLASSIFICATION OF URETEROPELVIC OBSTRUCTIONS

Analysis of ureteropelvic obstructions shows that they may be either extrinsic or intrinsic (Fig. 1). Extrinsic obstructions are kinking and distortion of the ureteropelvic outlet by

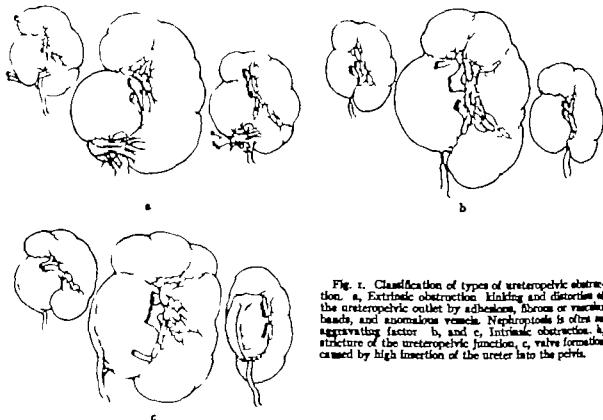


Fig. 1. Classification of types of ureteropelvic obstruction. a, Extrinsic obstruction: kinking and distortion of the ureteropelvic outlet by adhesions, fibrous or vascular bands, and anomalous vessels. Nephroptosis is often an aggravating factor. b, and c, Intrinsic obstruction. b, stricture of the ureteropelvic junction, c, valve formation caused by high insertion of the ureter into the pelvis.

adhesions fibrous or vascular bands and anomalous vessels. Intrinsic obstructions may be subdivided into two types (1) stricture at the ureteropelvic junction, and (2) valve formation caused by high insertion of the ureter into the pelvis. Thus, for clinical purposes obstructions at the ureteropelvic junction may be divided advantageously into three types or groups. As Deming has tersely stated,

Causes of intrinsic obstruction at the ureteropelvic junction are a thickening of the musculature, the development of hyperplastic fibrous tissue and a fibrous contracture producing a small stoma. **Causes of extrinsic obstruction** are strands of fibrous tissue running across the ureter at the junction and aberrant vessels. In a series of 82 cases he found intrinsic lesions in 37 and extrinsic in 50, of which 24 were due to bands of fibrous tissue and 26 to anomalous vessels. It must be borne in mind that these groups may overlap and it is not uncommon to find in a given case a combination of intrinsic and extrinsic factors at work. This fact led Henline and Menning

to emphasize the necessity during surgical exposure of measuring the inner caliber of the ureteropelvic junction which cannot be judged accurately by external inspection or palpation. Thus after removal of extrinsic factors one should open the pelvis through a small incision and calibrate the outlet. This step can be done very readily by passing the tip of a Mayo hemostat or a bougie No 12 to 14 F down through the ureteropelvic junction and will reveal any intrinsic obstruction.

METHODS OF PYELOPLASTY

A large number and variety of ingenious pyeloplastic procedures have evolved for the correction of obstruction at the ureteropelvic junction. The author has gathered together the principal ones which have become more or less standardized and are in current use (Figs. 2 to 8 inclusive). Analysis reduces them essentially to four basic methods:

1. Reimplantation of the sectioned ureter into the pelvis at its most dependent part

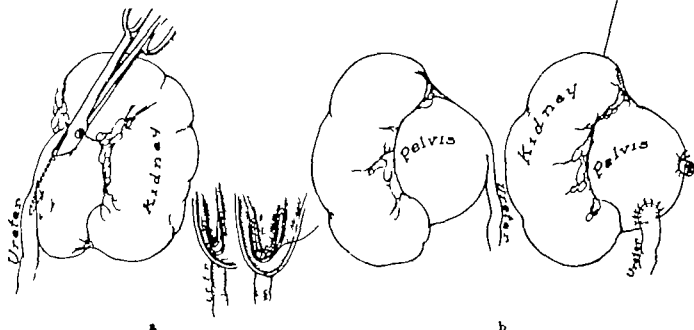


Fig. 2. a, The first recorded pyeloureteroplasty (Trendelenburg, 1886). The ureteropelvic valve is cut downward with scissors, through high incision in pelvis. The cut

edges of the ureter are sutured to the cut edges of the pelvis (inset). b Kuester 1893 reimplantation of ureter ureteropyelonecstomy

(Kuester) with or without excision of redundant pelvis.

2 Longitudinal incision with transverse closure (Fenger)

3 Y incision with V closure (Schwyzer Foley)

4. Lateral anastomosis of pelvis and ureter
The fourth type is essentially the original Trendelenburg operation. The Finney pelvio-ureteroplasty and Priestley's procedure which includes excision of redundant pelvis, are interesting and useful variations of the same fundamental principle

CAUSES OF FAILURE

In evaluating pyeloplastic procedures, it is necessary to pool the experience of many surgeons because no operator has had sufficient experience with all types to determine their relative merits with any degree of authority. No single method has proved uniformly successful. Various statistical reviews indicate failure in as high as one third of cases in some series. Ormond states that nephrectomy is too frequently performed because of unfamiliarity on the part of the profession with the conservative operations that can be effectively

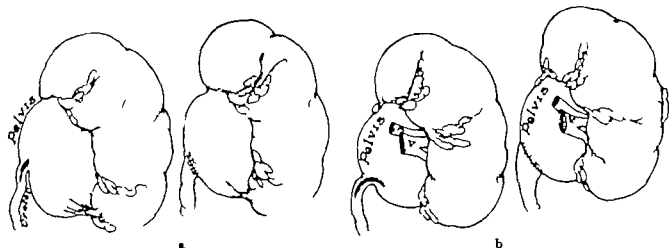
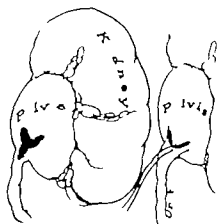
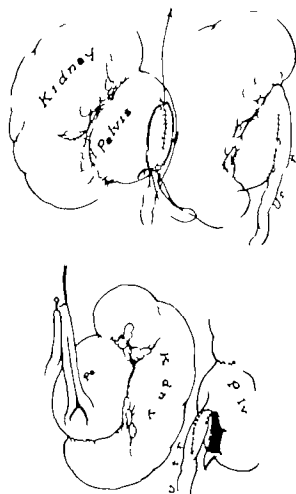


Fig. 3. Pelvioureteroplasty a, Pyeloplastic procedure of Fenger 1892, adaptation of the Heineke Mikulicz principle. b, Modification similar to Finney pyeloplasty



b

Fig. 4. a, Pyeloplasty of von Lichtenberg, similar to Flannery pelvioureterostomy without section of ureter. Von Lichtenberg's method, 920, with long incision of the ureter and hydronephrotic pelvis and double line of suture as in gastroenterostomy. b, Schwytzer procedure, 1935, pelvioureterostomy, so called Y plastic, and c, Foley modification, 1937 of Schwytzer operation.

employed lack of confidence by some surgeons in pyeloplasty as a remedy for hydronephrosis, disinclination to run the risk of failure with the embarrassment of having to do a nephrectomy at a later date disagreement concerning the preferable type of repair and insufficient standardization of technique. Reasons for failure of plastic operations on the kidney pelvis are enumerated by Lubash as follows: (1) leakage of urine and perirenal infection at the point of anastomosis (2) tension along the suture line with secondary infection (3) puckering and buckling at the line of anastomosis (4) new stricture formation acting as a boomerang (5) retention of urine and secondary pyelonephritis or cortical abscess formation (6) persistent urinary fistula.

Growing experience during the past few years has shown how these pitfalls may be

avoided. The fundamental principles essential to success have been elucidated so that at the present time pyeloplasty may be undertaken with far greater assurance of a successful outcome and nephrectomy need be contemplated only in cases in which hydronephrosis is so advanced that merely a thin walled sac remains or unyielding chronic infection is present. Even in such extreme cases remarkable results may sometimes be achieved by plastic repair particularly in solitary kidney which offers no alternative operative procedure. In such cases pyeloplasty may be a life saving measure as shown in Case 1 (Fig 12) and Case 2 (Fig 13).

SELECTION OF CASES

Poor results following pyeloplastic procedures are due not so much to the particular

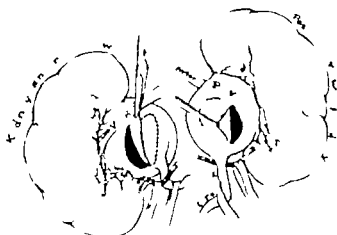
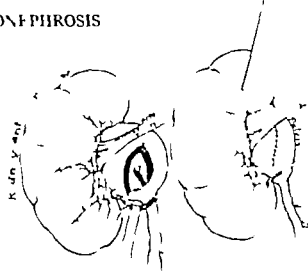


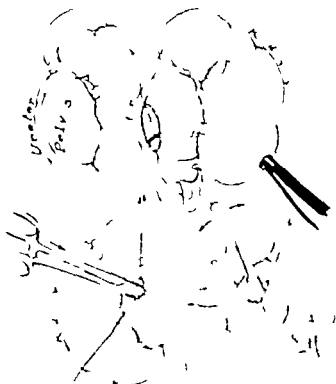
Fig 5 Pyeloplasty of Young 1932 with partial excision of anterior and posterior walls of pelvis to reduce size of



pelvis and realign ureter so as to avoid sacrifice of aberrant blood vessels to lower pole of kidney

method employed but rather to improper selection of cases and failure to appreciate certain fundamental surgical principles essential to success. Whether to perform radical (nephrectomy) or conservative (pyeloplasty) surgery is not always an easy decision to make. On the basis of renal counterbalance Hinman states that the most skillfully performed and technically perfect plastic repair of a unilateral hydronephrosis with a normal compensatory mate is the wrong solution if it fails to put this side in the position of potential ability to carry the total load should it ever become necessary. One-quarter of the total renal mass will support life. Therefore a hydronephrotic kidney which cannot perform 25 per cent of total function is not worth saving, although occasional exceptions may justify preserving a kidney with some 10 to 15 per cent of total function. This view would seem logically correct if one could guarantee the future integrity of the healthy compensatory mate. However the possibility of some intercurrent pathology overtaking the sound contralateral organ and causing impairment of its function cannot be completely ignored. The increment of function of the repaired hydronephrotic kidney however small might contribute sufficiently to the total function to sustain life. Consequently the fear that some catatrophic might occur which would impair the function of the good kidney prompts some urologists to perform pyeloplasty rather than nephrectomy even in advanced cases.

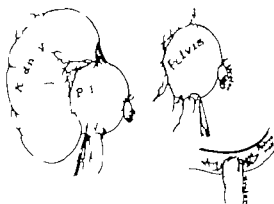
With respect to determining the functional ability of the hydronephrotic kidney Hinman states that unilateral hydronephrosis will show its full capability at the first test (if the kidney is active uninfected and draining freely). He further asserts that the first test will be as good as any subsequent ones even



I got a letter by express in that post yesterday morning
 stating that the Government had decided to put the
 railway station at Ramnagar. I told you that I had written to the
 public opinion in the Government and that I had written to the
 Government to put the station at Ramnagar. I told you that I had
 written to the Government to put the station at Ramnagar. I told you
 that I had written to the Government to put the station at Ramnagar.



Fig. 7 a. Pyeloplasty of Priestley (1930) with excision of pelican-like pouching of the pelvis. This procedure is an improvement over the original Trendelenburg pyeloplasty.



b

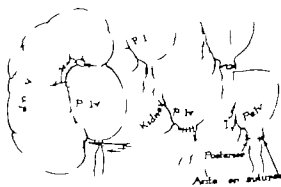
b. Pyeloplasty of Lubash (1937) ureteropyelostomy. This procedure is an elaboration of the original Kustin operation.

though the catheter may be retained for weeks. This is important because an uninfected hydronephrosis should not be exposed to the very considerable risk of infection which a retention catheter carries. It is, therefore, preferable to repeat ureteral catheterization and to study relative function. There are many urologists of great if not equal experience who take exception to these views including the statement that the function years after repair will be the same as at the time of repair, no more no less, with the opposite normal kidney.

From a more limited personal experience in determining the proper course of action, the tendency has been to depend less on relative function studies which are subject to many variables and more on the following three factors: absence or presence of infection and its severity, the pyelogram, and the appearance of the kidney at operation. One is surprised at times to find at operation an amount of parenchyma considerably in excess of that indicated from studies of function. In any event, no treatment is justified which is not based on the most complete urologic investi-



Fig. 8 a. Pyeloplasty using Kustin principle of ureteropyelostomy but with radical excision of redundant pelvis. Radical resection of pelvis and ureter with reanastomosis of ureter to lowermost part of pelvis. This



b

operation is used extensively by Priestley and others in cases of extrarenal pelvis with constriction and distortion of upper ureter. b. Pyeloplasty applying Tenger (Gibson) operation to opposite sides of ureteropelvic junction.

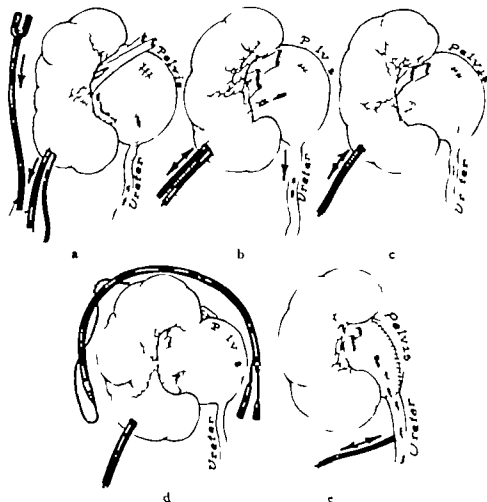


Fig. 9. Methods of ureteral splinting and nephrostomy drainage. a, urethral catheter No. 10-24 T tube at 1 ft b Double eye Robinson urethral catheter No. 0-13 c Cumming nephrostomy tube d, McIvor nephrostomy tube e Ureterostomy splinting and drainage with T tube advocated by Davis and Deming

gation and it is usually wise to balance the findings of one complete study against those of a second confirmatory study. Sargent stressed the tendency of hydronephrosis to be bilateral and for the opposite kidney in some instances to become hydronephrotic following nephrectomy. Care too must be observed in determining that the obstruction is actually at the ureteropelvic junction and not as Hunner has so often emphasized at some point in the lower ureter.

CHOICE AND TECHNIQUE OF PLASTIC REPAIR

Adequate exposure is essential for the proper execution of pyeloplasty. As a result of the teaching of Hess, a loin incision is made directly down on the twelfth rib which is resected. This incision not only permits excel-

lent exposure of the kidney but affords less chance of injuring nerves supplying the abdominal wall. Exception is made in cases of nephroptosis in which good exposure can be obtained without removal of the rib.

The proper choice of plastic operation will depend upon whether the hydronephrosis is caused by Type I, II or III obstruction. The correct classification can sometimes be surmised during preliminary investigation but can be definitely determined only at operation. The first requirement is, of course, removal of all obstructing fibrous bands and adhesions and division of aberrant vessel—in other words a thorough pyeloureterolysis. This may be all that is necessary to eradicate completely the obstruction to drainage proving that the lesion is extrinsic (Type I). In per-

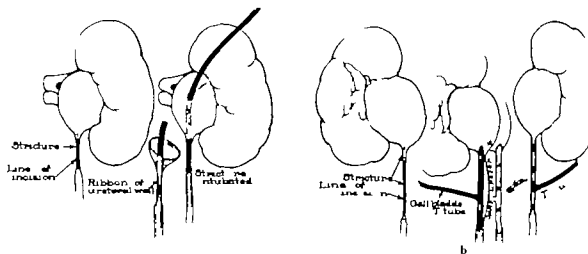


Fig. Intubation pyeloureterostomy methods of Davis.

sonal experience about 50 per cent of cases fall in this category. However, as previously emphasized, the lumen of the ureteropelvic junction should be calibrated before concluding the operation and ureteral splinting resorted to if there is much peripelvic and

perureteral fibrosis with angulation or distortion of the upper ureter.

If the obstruction is intrinsic it will fall in either Type II or III. One then proceeds with an appropriate pyeloplastic operation as illustrated by Figures 2 to 8 inclusive. For

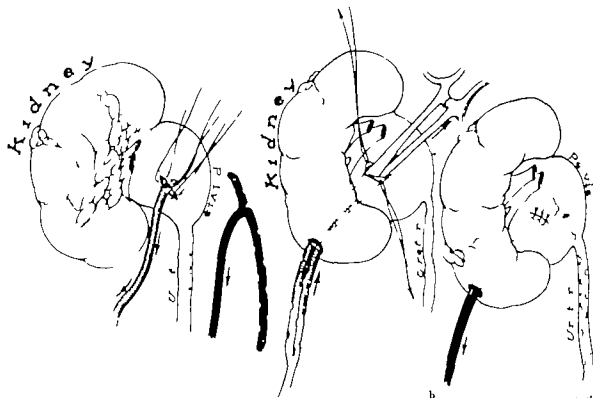


Fig. Methods of splinting (or intubation) and drainage with T-tube which is now used by the author. T-tube

lends itself readily to use following all types of plastic operations.

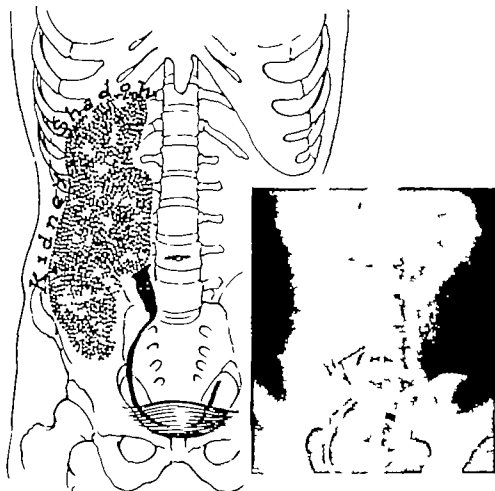


Fig. 3 Case 1: Congenital solitary right kidney. Female aged 24 years, had chronic infected hydronephrosis of giant proportions, causing externally visible abdominal tumor. On cystoscopic study it was impossible to pass catheter of free pyelographic medium beyond ureteropelvic junction. Condition of patient was grave due to uremia. At operation kidney was found to be a thin-walled translucent sac with apparently insufficient parenchyma to sustain life. Davis-Rammstedt pyeloplasty was performed with ureteral splinting and nephrostomy drainage with McIvor tube. This tube did not maintain its splinting action long but crawled back into hydronephrotic sac. Nevertheless, patient recovered and reports fair health 1 year later. Large catheters can be passed readily up ureter into kidney pelvis.

Type II obstruction (Fig. 1) consisting of stricture of the ureteropelvic junction the procedure preferred by the author is the Davis-Rammstedt operation because of its simplicity, ease of execution and excellent results (Fig. 6). The pelvis is opened between stay sutures a Mayo hemostat is pushed down through the ureteropelvic junction and the jaws are spread gradually until the lumen is more than adequate. Simultaneously a row of parallel vertical incisions is made about the outside down to the mucosa in order to divide constricting muscle fibers and scar tissue. This step is followed by splinting or intubation (Figs. 9, 10 and 11) to maintain

the caliber of the lumen at No. 12 to 14 F until healing is complete. Other plastic operations such as the Fenger procedure, the Finney pelvoureteroplasty, the ureteropyeloneostomy of Kuester or Lubash or the Schwytzer Foley methods may be used with success in Type II obstruction.

For Type III obstruction involving valve formation with high insertion of the ureter in the pelvis, the original Trendelenburg operation modified (Fig. 2) is still eminently satisfactory. This method was used in the cases illustrated in Figures 12 and 13 with good results. If there is much pouching of the lower pelvis the method of Priestley (Fig. 7) has

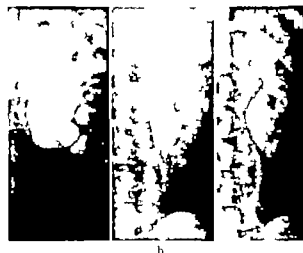


Fig. 3 Case a. Preoperative pyelogram. Congenital solitary left kidney complicated by acute fulminating colon bacillus pyelonephritis. Female, aged 5 years. Inability to maintain catheter drainage and grave condition of patient made emergency operation necessary. Hydro-nephrosis due to Type III ureteropelvic obstruction was found to be complicated by edematous adhesions and aberrant vein. Pyeloureterolysis with sacrifice of aberrant vessel and Trendelenburg plastic was performed. No sutures were used due to necessity for haste and friable nature of tissues. Ureteral splinting and epistomy were maintained 3 weeks. Complete recovery. b. Pyelogram 6 months, and c. 4 years after operation. Ureter now taut and free from pus cells intra muros phenolsulfonphthalein, 60 per cent in 1 hour. This case strikingly illustrates the value of pelvoureteral splinting and lends support to Davis' view of the importance of intubated ureterotomy.

ment. In Type III one may also use the reimplantation methods of Kuester or Lubash or lateral anastomosis procedures as shown in Figures 3, 4, and 6 including that of Foley. In patients with excessively redundant pelvis radical excision of the pelvis with reanastomosis of the ureter to its lowermost part (Fig. 8) may be practiced. In cases of anomalous artery too large to sacrifice the procedure of Young (Fig. 5) or ureteropyelostomy (Figs. 2 and 7) may be utilized to advantage. In general No. 00000 chromic catgut mounted on atraumatic needles seems to be the suture of choice in plastic procedures. However, the author regards adequate splinting or intubation as more important in obtaining a good result than the most meticulous suturing.

The problem of sacrificing an anomalous vessel requires careful consideration. Anomalous veins may be sacrificed with equanimity but arteries are terminal without anastomoses,

so that a localized area of anemic necrosis results from their loss which may become infected and jeopardize the success of the operation. Shupe reported an interesting exception to this rule in a case in which resection of a slate pencil sized artery extending from the aorta to the lower pole of the kidney did not result in development of an infarct. The lesson to be derived is that it is safer to divide an aberrant vessel to the kidney arising from any source other than the renal artery. Since nephropoiesis is a complicating or aggravating factor in a certain percentage of cases of all types, nephropexy should be performed as a part of the operative program when indicated. Renal sympathectomy is occasionally included in the treatment when the obstruction appears to be more dynamic than mechanical in nature in order to make doubly sure of relieving pain.

URETERAL SPLINTING AND INTUBATION

Consideration of the value of ureteral splinting and intubation with its necessary corollary—nephrostomy, pyelostomy or ureterostomy drainage—has been purposely reserved until now. In spite of certain dissenting voices, personal experience has led to the conviction that this is the most important single factor in obtaining with certainty a successful end result in the highly technical field of pyeloplasty. It is doubtless true that splinting or intubation is not always necessary but general opinion differs from that of Deming who states that splints are unnecessary and who resorts to drainage only in infected cases. In a communication published in 1939, the author emphasized the value of ureteral splinting following operations on the kidney in which the upper ureter and pelvis are surrounded by dense adhesions causing kinking, narrowing and distortion. Just previous to that time failure to utilize splinting in three consecutive cases resulted in the necessity of performing secondary nephrectomy in one. In the other two ureteral dilators entered the pelvis of the kidney with the greatest difficulty after operation. The following conclusion was reached: it should be axiomatic that the urologist make use of ureteral splinting following operation on all cases of ureteral and renal

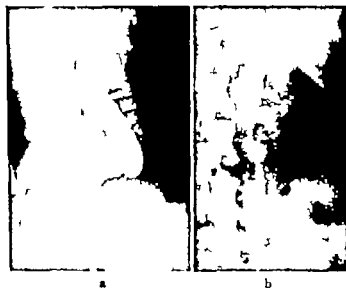


Fig. 14. Pyelograms, a, before pyeloplasty and b 3 weeks after showing slight leakage at site of plastic operation

calculi in which dense adhesions or other types of obstruction to free drainage either intrinsic or extrinsic exist about the ureter or pelvis. The author has come to consider this as the most important fundamental surgical principle essential to success in plastic operations for hydronephrosis as well.

The value of the ureteral splint has been emphasized by Peck and later by Harris, Cabot, Moore, Sargent, Priestley, Sharp and others. More recently Davis has reported on the value of intubation which he utilized ingeniously in exceedingly difficult cases. His results were so spectacular that his intubation technique has taken precedence at the Jefferson Hospital over all plastic operations on the ureter and ureteropelvic junction (Fig. 10).

The principal methods of splinting intubation and drainage are shown in Figures 9, 10 and 11. Personal experience with the Cumming and McIver nephrostomy tubes has been unsatisfactory. One reason is that the splinting portion of the tube which goes down the ureter is not sufficiently rigid and tends to crawl back into the pelvis (unless the pelvis has been resected) where it coils and completely defeats its purpose. When I visited Deming at Yale in February, 1940, he called the T tube to my attention. Since then I have used it in various ways as shown in Figures 9 and 11 and have come to depend on it more and more following plastic operations for



Fig. 15. Ureterograms, a (retrograde) preoperative, and, b (excretory) 5 years postoperative. Female aged 25 years, had left calculous hydronephrosis associated with nephroptosis. Pyeloureterolysis, pyelolithotomy and nephropexy without splinting produced this obviously excellent result.

hydronephrosis as well as for drainage when required in other types of renal surgery. It can be used in a number of ways with the greatest facility; it can be cut to measure so to speak, and is easily introduced and removed. I wish to draw attention particularly to the fact that one should always cut out a V opposite the stem of the T not only to render it easily collapsible but also to enable visualization of the opening into the stem. Not infrequently one will find a small flap of overlapping rubber across the opening which can be readily removed so it will not interfere with drainage or irrigation. Multiple openings to facilitate drainage are cut in the T tube as shown in Figure 11. Some writers have expressed objections to nephrostomy drainage because of the danger of infection and secondary hemorrhage. No personal difficulties of this sort have so far been encountered but for conscientious objectors the T tube lends itself just as readily to pyelostomy or ureterostomy drainage (Figs. 9 and 11). Splinting and drainage should be maintained for a period of 10 days to 3 weeks or more postoperatively depending upon the apparent needs of the individual case.

Proper evaluation of the end results of plastic repair of ureteropelvic obstructions causing hydronephrosis depends on careful

follow up studies including urography at regular intervals. These examinations have the added advantage of making available early detection and treatment of residual infection or subsequent obstruction. Deming warns against too immediate postoperative ureteral catheterization. A personal case is shown in Figure 14 in which a catheter was passed 3 weeks after operation. The pyelogram reveals some leakage at the site of pyeloplasty but fortunately no harm came of it. Figure 15 shows the remarkable ability of the kidney to return to normal following removal of obstruction.

SUMMARY

It has been the author's aim in this communication to review the subject of hydronephrosis due to obstruction at the ureteropelvic junction to describe the three general types of obstruction and to gather together the principal methods of pyeloplasty in current use. It is hoped that this may serve as a basic reference for the future standardization of plastic procedures.

Experience with pyeloplastic repair suggests the possibility of eliminating the elaborate plastic operations and the delicate suturing they entail in favor of the simpler methods. The value of pyeloureteral splinting and intubation in selected cases is re-emphasized as an insurance against failure. It is even possible that these procedures may supersede to a large extent plastic operations

on the ureter and ureteropelvic junction. At the present time we know that pyeloplasty and ureteral splinting or intubation are effective when used conjointly. Future experience will determine their relative rôles, as well as the comparative merits of the various methods of pyeloplasty.

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SICKLE FLAP FOR NASAL RECONSTRUCTION

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FREQUENTLY one sees a patient on whom a beautiful operation has been done to reconstruct a portion of the nose but the color of the reconstructed part does not match that of the rest of the nose or if the material for the reconstruction has been used from some other part of the face the donor area stands out with conspicuous scarring or a discolored skin graft that detracts greatly from the end result. To be able to obtain material for reconstructing the tip or an ala of the nose from the forehead and at the same time to create very little noticeable defect at the donor site is the advantage of the flap that I am describing.

When a portion of the nose is replaced by a plastic operation the skin of the new part should blend in size, shape, color and texture with that of the rest of the nose, but in addition the donor area from which the flap is obtained should not show noticeable scarring or

From the Section on Laryngology, Oral and Plastic Surgery, Mayo Clinic.

Read before the meeting of the American Association of Plastic Surgeons, Philadelphia, Pennsylvania, May 4-7, 1941.

a skin graft that detracts from the result obtained on the reconstructed part. Study and planning of flaps and procedures are necessary to obtain such a result. While many of the minor defects of the ala and tip of the nose may be corrected by sliding flaps or delayed flaps about the nose and cheek with or without the use of a skin graft, the larger defects of the ala and tip require more material than can be obtained in this way. The skin from the forehead has been used for many years for these purposes and is a good match with the skin of the nose. A flap from the cervical region or from the arm as a rule does not blend well with the rest of the nose. The forehead flap used with the supraorbital vessels or the anterior branch of the superficial temporal artery usually leaves considerable scarring on the forehead and also a noticeable patch where the free full thickness skin graft is used to replace the skin used for nasal reconstruction.

In order to avoid this scarring and to obtain a pedicle flap contiguous with the area to be grafted, I have employed a flap in the temple



Fig. a Postoperative defect of the left ala and tip of the nose 1 year after removal of a postulated epidermoid with surgical diathermy. The sickle flap has been elevated and the forehead end has been lined with a skin graft. b The lined flap has been brought down to the nose. The flap has been tubed by means of petrolatum fine mesh

bandage. A skin graft has covered the defect in the scalp and forehead. c The flap has been replaced. Not the reconstructed part of the nose and the small area of skin graft on the forehead which can readily be covered with the hair. Photograph made 2 weeks after the last stage of the operation.

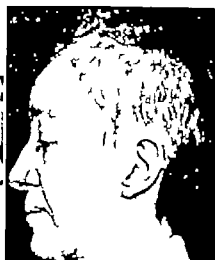


Fig. 2. a, Postoperative defect of the lower half of the nose 3 years after removal of a postinfiltrated epithelioma with surgical diathermy. b, The sickle flap has been elevated and delayed and the distal end has been lined with

skin graft. c, The flap has been returned. The small defect where the skin graft is present at the mesial end of the flap may be noted. Sutures have just been removed from the reconstructed nose.

scalp and forehead. The flap is sickle-shaped and usually about 3.5 to 4 centimeters in width. Beginning just above the zygoma in front of the ear it runs backward and upward with the parietal branch of the superficial temporal artery in the pedicle and then curves forward on the forehead to the bay of skin just below the hairline which is present in most persons just lateral to the midline. The skin in this area is what is used for the reconstruction and may be enough for half a nose, an ala or a

tip. For total rhinoplasty I usually prefer an up-and-down forehead flap using the supra-orbital vessels on one side as the pedicle. The distal end of the flap from the opposite side of the forehead forms the nose after the method of Gillies. However I have used the sickle flap in total rhinoplasty with success.

METHOD OF USE

In the using of the sickle forehead flap for nasal reconstruction it is necessary to follow



Fig. 3. a, The defect in the right side of the nose and cheek and inner canthus may be noted. There is loss of the right half of the nose and of a portion of the bridge and of the cheek. A sickle flap has been elevated and the distal end has been lined with skin graft to line the part of the flap that will reconstruct the ala and right side of the nose. b, The flap has been brought down to the nose. That part which is to reconstruct the nose is lined with skin graft. The flap has been tubed by means of fine mesh gauze band-

age. c, The defect in the forehead and scalp has been skin grafted. The flap has been tubed by means of fine mesh gauze bandage. Before being replaced, flap is cut half way across and then resutured so the point can be sutured to cheek in order to insure the blood supply on the new skin over the nose. d, The flap has been replaced and stretched so that it is not necessary to leave more than a small skin graft on the forehead below the hairline. The reconstructed portion of the nose has been sutured to the cheek.

the delayed flap technique in order to insure the blood supply. Careful planning is essential so that material obtained will be of the right size and shape and free from hairs. The area to be employed is marked out with blue pencil on the forehead just lateral to the midline and just below the hairline. Then the hair is shaved and a flap is marked out with indelible pencil adhesive tape or gauze bandage being used as a pattern so that the flap is of sufficient length at the time of operation. One must remember that the lower margin of the flap determines its length so that it should be made long enough. The flap is elevated both pedicles being left intact. At this time or at a second stage the mesial end of the flap may be lined with a shaved skin graft as in the making of an ala so that it will have skin on both sides. The forehead end of the pedicle is cut across at its subsequent stage to the skin grafting of the lining and then at a later stage the flap is brought down to the defect in the nose. It may be advisable to make one complete elevation of the flap before bringing it down in order to insure the blood supply.

If the flap is to be employed to reconstruct the lower half of the nose including the tip and columella and has to be folded on itself. I feel that a better shaped nose is obtained if the bringing down of the flap is delayed until 3 months after the flap has been prepared. In this way when the flap is brought down it is very thin and folds readily. It makes a better shaped nose than if it has been elevated and brought down when it is quite thick and difficult to fold. When the flap is brought down it is an open flap and is converted into a closed one by wrapping with 2 inch (5 cm) gauze bandage. This also protects the eye for 2 or 3 days from the hair bearing flap until it sags down on the cheek. At the time of the operation the raw surface on the forehead is completely covered with a shaved graft. After the flap has been in place for 2 weeks the point in



Fig. 4. a, left Defect following removal of postirradiated squamous cell epithelioma of the nose. This was replaced with a lined sickle flap from the scalp and the forehead. b, It was possible to stretch the replaced flap so that the small area of the skin graft that was left was excised 3 months later without leaving any grafted area on the forehead. The skin of the reconstructed portion of the nose matches in color and texture with that of the rest of the nose.

the flap that will form the distal margin of the reconstructed part is cut half way across and sutured and then a week later it is completely cut across and the pedicle and distal portion of the flap are replaced on the forehead after removal of the skin graft. In many cases it is possible to stretch the flap so that the entire skin graft may be replaced with the flap thus leaving no skin graft visible at the lower margin of the hairline. This lowers the hairline a little but in most cases not enough to be noticeable and I feel that it is a distinct advantage. If it is impossible to remove all the skin graft the lower and mesial portions of it which remain may be excised at a secondary operation.

Figures 1, 2, 3 and 4 illustrate the various steps in the procedure.

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TABLE I—SEX INCIDENCE OF FIBROSARCOMAS AND BENIGN TUMORS OF THE SUBCUTANEOUS TISSUE AND FASCIA

	Males	Females
Fibrosarcomas	68	43
Fibromas	66	76
Lipomas	133	220
Hemangiomas	56	82
Lymphangiomas		12
Angioendotheliomas	20	10
Neurofibromas	18	13
Neurilemmomas	11	20
Keloids excluded		

AGE

The age incidence of fibrosarcomas in our series closely paralleled the age incidence of benign fibromas (Table III). Although usually stated as being a disease of past middle life they have been reported as occurring at all ages. In our series an almost equal distribution occurred between the ages 10 and 70, the average age being 36.4. The youngest was 2 years of age and the oldest 80. Quick and Cutler reported an equal distribution between ages 30 and 60. Meyerding, Broders and Hargrave in their series of 152 cases with fibrosarcoma of the extremities found the average age incidence to be 43.2. Hudson described a case of intrauterine fibrosarcoma of the foot. Table III shows the age distribution of fibrosarcomas as compared to other benign tumors of the subcutaneous tissue and fascia.

RELATION OF TRAUMA

There is evidence to support the view that trauma may be a factor in the formation and acceleration of many benign subcutaneous tissue tumors. This is especially evident in studies of fibromas arising from the abdominal wall in operative scars (Fenick) and on the hands and feet. Mankin in his studies of 629 neoplasms of the anterior abdominal wall reported 423 fibromas and 155 fibrosarcomas. Of these 629, 544 were women, 90 per cent of whom were parous, and in 62 per cent of whom a definite relationship between pregnancy and origin or acceleration of growth was found to exist. Waugh in 55 cases of fibroma of the abdominal wall found a close association with pregnancy in 25 cases, trauma in 6 cases, and surgical incisions in 15 cases.

The relationship of trauma to the formation or acceleration of fibrosarcoma is doubtful.

TABLE II—RACE INCIDENCE OF FIBROSARCOMAS AND BENIGN TUMORS OF THE SUBCUTANEOUS TISSUE AND FASCIA

	Colored	White
Fibrosarcomas	39	92
Fibromas	44	98
Lipomas	98	270
Hemangiomas	12	126
Lymphangiomas	6	13
Angioendotheliomas	6	31
Neurofibromas	13	18
Neurilemmomas	3	20

Occasionally a fibrosarcoma occurs in an area subjected to repeated trauma (Quick and Cutler). Rarely do they occur in old burn scars or in indolent ulcers (Fleming and Rezek, Glasser). Single episodes of trauma are frequently associated by patients with the appearance of a fibrosarcoma. In our series 3 patients gave a history of a single episode of trauma followed in a short period of time by a fibrosarcoma. Not infrequently patients gave a history of a single episode of trauma followed by edema, discoloration and a small subcutaneous nodule which persisted for years and then began to grow rapidly following another slight injury or with no subsequent trauma. Biopsy would reveal fibrosarcoma. Meyerding, Broders and Hargrave reported 17 out of 152 cases of fibrosarcoma which were associated with trauma. Quick and Cutler reported 14 of 72 cases with a history of trauma. Case reports of fibrosarcomas occurring after a single episode of trauma are becoming increasingly more numerous (Blake and Bradford, Zuckerman, O'Brien).

A simple fibroma may occasionally be the site of origin of a fibrosarcoma (Fahr, Geschickter and Lewis). Unfortunately, one rarely has more evidence than the patient's history to corroborate this fact and from a histological standpoint it may be difficult to differentiate between a low grade fibrosarcoma and a simple fibroma (Fig. 1). Case 3 offers an illustration.

W. J., a 30 year old white man was first seen September 1931 with a tumor of the left hand measuring 5 by 4 centimeters. He gave a history of gradual enlargement over a period of 10 years with some recent increase in growth. Local excision was performed September 6, 1931. The pathological report was simple fibroma with calcification. Three months later the patient noted the recurrence of a



Fig. 1. Fibrosarcoma of the hand in 30 year old hit man. The history of gradual enlargement over period of 30 years. Histological section shows irregularity of simple fibroma.

small nodule the size of a pea. The growth was rapid. A 1/2 inch x 1/2 inch x 1/2 inch section was performed and the patient was left with a full thickness graft. The tumor again recurred 3 months and Oct. 1933 the left hand was amputated. The patient died 34 months later in pulmonary metastases.

CROSS CHARACTERISTIC

Fibrosarcoma arises most frequently in the subcutaneous tissue and fascia and less frequently in the tendons, dermis and muscle. Fibrosarcoma have been reported arising primarily in the heart (16, 23, 37), kidney (36), epididymis (5), prostate (34), adrenal gland (11), stomach (9), ileum (2), lung (8), bronchus (6), brain (10) and larynx (7, 31).

Fibrosarcoma appears to have a predilection for certain topographical areas of the body occurring more frequently around the upper thigh and shoulder region and to a lesser extent around the knee and elbow (Table IV). The reason for this is not evident. The tumors are usually densely adherent to the fascial septa extending deep between the muscle groups but occasionally completely encased within a single muscle (Fig. 2).

Rarely can a definite nerve origin be demonstrated although nerves and blood vessels running in the fascial septa may be included within the growth. All too frequently it is impossible to determine the specific site of origin (Fig. 3).

The tumors are usually single but occasionally multiple nodules may be found in the subcutaneous tissue. These probably represent metastatic lesions. Fibrosarcomas are usually rounded or lobulated and vary greatly in consistency from a stony hard fibroid like texture to a soft lipomatous consistency. The gross character reflects the microscopic appearance, being dependent upon the relative cellularity of the tissue, the amount of microcellular and fibrous intercellular substance, edema, and hemorrhage. On section the acellular fibrous growths cut with a hard rubber sensation and reveal a fasciculated arrangement. The more cellular tumors present a homogeneous cross section divided into lobules by fibrous septa and numerous blood vessels.



Fig. 2. Fibrosarcoma encased within long flexor muscle removed from the thigh of 37 year old hit man.



Fig. 3. Fibrosarcoma of the foot in a 44 year old colored female treated by amputation. Case illustrates difficulty in determining specific origin.

Fibrosarcomas grow expansively and in a major portion of cases appear to be encapsulated (Fig. 4). Invasion of the surrounding tissue is however the rule and local recurrences result when excision within the false capsule is attempted. The tumor may invade and destroy the adjacent bone or the skin with resulting ulceration secondary infection hemorrhage and anemia. Extension into vessels accounts for frequent distant metastases (13).

The gross measurements of fibrous tissue tumors would appear to aid greatly in the diagnosis of border line cases when the microscopic picture is difficult to interpret. In our series 90 per cent of fibrosarcomas measured over 5 centimeters in diameter when the patient first presented themselves for examination whereas 85 per cent of fibromas measured under 3 centimeters. Only 13 of the 142 fibromas measured over 5 centimeters in size and of these 2 recurred and were later reclassified a fibrosarcoma. were fibromyxomas and

desmoid tumors of the abdominal wall. Only 3 of 31 neurilemmomas measured over 4 centimeters in size.

MICROSCOPIC CHARACTERISTICS

Fibrosarcomas grade from very cellular anaplastic types to fibrogenic tumors difficult to differentiate from fibromas. In most cases the diagnosis is easily established from the microscopic structure and the presence of mitotic figures but in an occasional case the diagnosis is determined only by the subsequent clinical course (Fig. 1).

Fibrosarcomas have been classified as to their growth potentialities by Quick and Cutler, Geschickter and Lewis, Broders, Hargrave and Meyerding. Classification is based upon the differentiation of the cells as manifested by their ability to produce fibrillar intercellular substance by the number of mitotic figures and giant cells and by the relative cellularity and anaplasia of the tissue itself. Quick and Cutler designated as grade I those sarcomas made up of spindle cells lying in a dense stroma of intercellular substance, grade II as those composed of large spindle cells with little intercellular substance and grade III as those made up of small spindle cells arranged in a fasciculi arrangement or large irregularly shaped cells growing diffusely with little or no



Fig. 4. Left. Fibrosarcoma of the left shoulder in a 3

old colored male showing characteristic growth. Fig. 5. Metastases of the fibrosarcoma in the lungs of a 37 year old white female. Tumor put in for fibrosarcoma of the leg.

TABLE V. RESULTS OF TREATMENT

	Clinically cured	Long disease	Dead	Total
Grade I				
Local excision				
Amputation				
Biopsy and cure				
Total				
Grade II				
Local excision				14 (100%)
Amputation			2	3
Biopsy and cure				
Total			2	17
Grade III		3	6	9
Local excision	1			27 (100%)
Amputation			7	
Biopsy and cure				3
Total			7	30
Grade IV			3	3
Local excision				1 (100%)
Amputation				
Biopsy and cure				2
Total			3	3
Total	11 (100%)	3 (100%)	11 (100%)	25 (100%)

Included in this group are cases treated for recurrence since 1940

overlying skin is absent. Growth is slower and rarely do they reach the dimensions of a fibrosarcoma of the same duration. Because of their origin from the nerve sheath pressure on the tumor frequently causes pain to radiate along the distribution of the nerve. They occur more commonly in the neck from the brachial plexus and along the medial aspect of the arm from the ulnar and median nerves. Fibrosarcomas rarely occur at these sites.

Soft fibrosarcomas are frequently confused with lipomas which they closely resemble in consistency, size and expansile type of growth. Lipomas are more apt to occur in those areas of the body where adipose tissue is normally concentrated and as they increase in size frequently become pedunculated. Lipomas in unusual sites are more frequently misdiagnosed as fibrosarcoma than the reverse. Aspiration biopsy has proved an aid in these cases.

CLINICAL ASPECTS AND TREATMENT

The high mortality rate in patients with fibrosarcoma is due to the difficulties in the

management of this malignant tumor. These difficulties are due in part to the wide variation in rate of growth, the invasive character of the tumor and the tendency to blood stream metastases. In our series of 111 cases 11 had pulmonary metastases when first examined and 33 had had previous local excisions. The duration of symptoms varied from 1 month to 32 years (Fig. 6). The average duration was 1 to 3 years with local recurrence showing up as late as 15 years following the primary excision.

Of utmost importance is the early recognition of the malignant nature of the tumors and wide surgical excision. It is a general feeling that amputation in fibrosarcoma of the extremities will more often effect a cure than local excision. This is probably true however if amputation was generally adopted for fibrosarcomas of the extremities many limbs would be unnecessarily sacrificed (Table V). Amputation has usually been reserved for those cases in which local excision has failed or has not been applicable due to the extensive nature of

the growth. The decision between amputation and local excision should be based upon a careful evaluation of the clinical history, the speed of growth, the size, location, and the histological character of the tumor. Biopsy or wide local excision should be performed and histological sections studied before amputation is advised. If biopsy is performed at the time of amputation, the same care should be taken to avoid transplanting tumor cells into an uninvolved area as is taken in excising carcinoma. Local recurrences may result from failure to observe this precaution (Harrell and Valk). Highly malignant tumors of the extremities and those arising in or invading the periosteum should be treated by amputation. Acellular slow growing tumors arising in muscle and the musculofascial septa may be treated by wide local excision. Those arising in the dermis and subcutaneous tissue are preferably treated by local excision. Occasionally fibrosarcomas of the shoulder or thigh require interscapulothoracic or ileoabdominal amputation to secure a satisfactory margin of safety (24) (Fig 7).

X ray therapy in the treatment of fibrosarcoma is without appreciable value. Growth in an occasional case appears to be retarded but no cures have been reported. Patients should be warned of possible damage to normal surrounding structures and of retarded epiphyseal growth in young individuals (Doub) (14).

Radical dissection of the regional lymph nodes was performed in a few selected cases but the series is too small to draw any conclusions as to the therapeutic value.

RESULTS OF TREATMENT

In our series of 111 cases, 33 cases or 29.7 per cent, were listed as clinically cured. Of these 33 cases, 3 have been well over 11 years, 17 have been well 7 to 10 years, 10 have been well 6 years, 2 have been well 5 years, and 1 has been well 4 years (Table V). Eleven of these had had previous local excisions. Of 14 classed as grade I, 12 or 85 per cent are well, of 27 classed as grade II, 8 or 29.6 per cent are well, of 19 classed as grade III, 5 or 26.3 per cent are well, of 51 classed as grade IV, 8 or 15.7 per cent are well.

The mortality rate was 62.2 per cent. 81 per cent are still living with the disease or have had recent local recurrences treated.

The results with local excisions in grades I and II were satisfactory but amputation if possible would appear to be indicated in grades III and IV.

In 25 or 22.5 per cent, only biopsy was performed and x ray therapy given. Of these 25, 11 had pulmonary metastases, 3 had subcutaneous metastases, and 3 had lymph node metastases when first examined. Two are still living, one 8 years with a fibrosarcoma of the thigh and one 5 years with a fibrosarcoma of the jaw following x ray therapy.

SUMMARY

Eight hundred and seventy-one soft tissue tumors occurring in 80,000 surgical specimens examined during the years 1931 to 1941 were classified as to sex, race, age, anatomical distribution, and size. There were 111 fibrosarcomas, 142 fibromas, 358 lipomas, 142 hemangiomas, 17 lymphangiomas, 39 angioendotheliomas, 31 neurofibromas, and 31 neurilemmomas. The ratio of benign to malignant tumors was 8 to 1.

Fibrosarcomas occurred 68 times in males and 43 times in females, a ratio of 1.6 to 1. This was in contrast to the benign tumors which occurred more frequently in females or showed an equal sex distribution (Table I).

The race distribution showed a slightly higher incidence in white than colored patients (Table II).

Fibrosarcomas occurred with almost equal frequency between the ages of 10 and 70, being slightly higher between the ages of 30 and 40. The average age incidence was 36.4. The average age incidence for fibromas was 32.1 years and for lipomas 42.3 years.

Fibrosarcomas occurred more frequently about the thigh and shoulder regions. Fibromas occurred more frequently around the head, hands, and feet and legs and lipomas showed a higher incidence on the body (Table IV).

The 111 fibrosarcomas were classified according to the relative proportion of cells to fibrillar intercellular substance, the number of mitotic figures, the number of giant cells, and

TABLE V—RESULTS OF TREATMENT

	Classically cured	Living with disease*	Dead	Total
Grade I				
Local excision				
Amputation				
Roentgen and x-ray				
Total				
Grade II				6 (6%)
Local excision				
Amputation			8	18
Roentgen and x-ray				
Total			6	7
Grade III		5		17 (14.5%)
Local excision				
Amputation			7	
Roentgen and x-ray				3
Total				6 (17.1%)
Grade IV				6 (17.1%)
Local excision				
Amputation				18
Roentgen and x-ray				
Total	8			12
Total Total	12 (10.7%)	9 (8.1%)	6 (5.1%)	27 (23.9%)

*Included in this group are cases treated for recurrence since 1934.

overlying skin is absent. Growth is slower and rarely do they reach the dimensions of a fibrosarcoma of the same duration. Because of their origin from the nerve sheath pressure on the tumor frequently causes pain to radiate along the distribution of the nerve. They occur more commonly in the neck from the brachial plexus and along the medial aspect of the arm from the ulnar and median nerves. Fibrosarcomas rarely occur at these sites.

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The 111 fibrosarcomas were classified according to the relative proportion of cells to fibrillar intercellular substance, the number of mitotic figures, the number of giant cells and

the regularity or anaplasia of the cells. The histological character was found to be an accurate index of the growth potentialities and an aid to prognosis and treatment.

The mortality rate was 62.2 per cent. 29.7 per cent were well and 8.1 per cent were still living with the disease.

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ARTERIAL EMBOLISM

A Simplified Technique for the Removal of a Saddle Embolus at the Bifurcation of the Aorta with the Report of a Successful Case

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ARTERIAL embolectomy is one of the real emergency operations in surgery. In order to restore the arterial circulation the embolus must be removed within a few hours of the time of embolism before secondary thrombosis has developed distal to the embolus. A cold painful cadaveric appearing extremity without motor function or sensation becomes again within a few minutes a living part of the body and gangrene necessitating amputation is prevented.

The bifurcation of the aorta is not an uncommon site for the lodgment of an embolus. Pearse in 1933 found 34 cases in a review of 282 reported embolectomies. Many patients have developed bilateral gangrene because either this site has been considered inaccessible to the direct approach for embolectomy or it was felt that the patient due to his cardiac condition would not withstand the operation necessary to expose the aorta. McClure and Harkins in an excellent review of the literature on arterial embolism found and tabulated 19 cases of successful aortic embolectomy by 16 surgeons. The first one was reported by Bauer in 1913. Murray reported the cases of 4 patients operated upon by him the largest single group.

The purpose of this paper is to discuss the principles of embolectomy to report another successful embolectomy at the bifurcation of the aorta by a transperitoneal exposure and to describe a new method of arterial control and technique for the removal of the embolus which has been found to facilitate greatly the operative procedure.

PRINCIPLES OF EMBOLECTOMY

Embolectomy is not a difficult operative procedure provided certain principles are fol-

lowed. Any surgeon should be able to perform a successful embolectomy if he has mastered the art of meticulous atraumatic surgery. The adherence to the following six principles is considered of the greatest importance if a successful result is to be obtained. The first principle is that an embolectomy must be carried out at the earliest possible time following the lodgment of the embolus. It is one of the real emergency operations in surgery since a matter of a few hours may mean the difference between a viable extremity and gangrene. Too often the physician who first sees the patient does not realize this and it is not until the extremity is obviously gangrenous that he refers the patient to a surgeon. By then it is impossible to save the limb because of the formation of a secondary thrombus filling the arterial tree distal to the site of the embolism. This condition may develop as early as 9 hours from the time of embolism as reported by Linton.

The second principle is that a direct and adequate exposure of the artery at the site of embolism should be obtained. The most gentle manipulation of the involved artery is necessary if the embolectomy is to be successful since rough handling and poor technique due to inadequate exposure may produce irreparable damage with secondary thrombosis. It is impossible to determine by a review of the literature the percentage of successful results with any one method of exposure since successful cases frequently are not reported. The operative approach in the 19 successful cases reported by McClure and Harkins was transperitoneal in 5 cases extraperitoneal in 5 and retrograde in 7. In 4 of the latter group retrograde removal of the embolus was combined with milking of the iliac arteries. In 2 cases the operative approach was not stated. In summary there were 10 successful cases

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artery is the most common technique described in the literature. Allen, Danz, Key, Lund, Murray, and others. The chief advantage of this method is that either of the materials is always available in any operating room. There are disadvantages, however, which outweigh this advantage. In the first place, if direct traction is used, it is necessary to apply considerable force to occlude the arterial blood flow, since the pressure by the tubing or tape is applied only to the under surface of the artery. The vessel being an elastic structure tends to stretch so that it is necessary to angulate it to a considerable degree before the lumen is completely occluded (Fig. 4). This requires considerable force so that there is danger of fracturing the arterial wall. If the material is twisted at the same time traction is exerted (Key and Murray), less force is necessary. It is impossible to obtain complete control of the arterial flow in either case without the continual application of excessive force. The method is cumbersome and unwieldy since the usual embolectomy requires three points of temporary arterial occlusion: one proximal and two distal to the embolus, so that at least three hands are necessary to effect control of the arterial flow. In the small operative field used for embolectomy, the surgeon is handicapped for this reason; for his assistants will not be able to help him to the greatest advantage.

The method described by Winkle and Cabot, in which they occluded the aorta by tying it temporarily with a cotton tape ligature, is open to criticism because of the danger of fracturing the wall of the aorta. The placing of a short piece of rubber tube over the artery and incorporating it in the temporary ligature, as recommended by Gage and Ochsner, is an improvement in this method, but the ligature may be drawn too tight and thus damage the vessel wall. Another disadvantage to the ligature method of temporary arterial control is that it is necessary to sever the ligatures after removal of the embolus when the collateral circulation is being tested and it is being ascertained if all the embolus has been removed, following which new temporary ligature must be applied in order to suture the arteriotomy wound.

The use of a Crile arterial clamp (Fig. 5) has not been found to be satisfactory, as it is difficult to apply and release. In addition, it is dangerous since the clamp is tightened with a screw which allows an enormous mechanical advantage so that irreparable damage may be done to the vessel. Pearce, Lesser, and Murray advocate the use of rubber shod "bull dog" arterial clamps (Fig. 5). The advantage of these is that they do not traumatize the arterial wall and they may be readily applied and released. The chief drawback to them is that they may be dislodged readily or even slip off by themselves due to the slipperiness of the rubber covering. Furthermore, the jaws of the clamps may not be long enough to permit their use on the common iliac artery in doing an aortic embolectomy.

After these various methods were tried and their disadvantages were realized, a different type of arterial control was developed. The ideal method of occluding an artery is to flatten it by opposing one side of its lumen against the opposite one (Fig. 4). In order to obtain this type of occlusion without danger of having the clamp slip off at a crucial moment, the Bethune lobectomy tourniquet (Fig. 6) has been utilized. This is a modification of Shenstone's tourniquet. It consists of a T-shaped metal rod with notches on it into which fits a ratchet that may be moved up and down on the rod. There are two apertures in the short limb of the T through which a heavy braided cotton cord passes, forming a loop. The two ends of the cord are tied to the ratchet so that the loop may be made large or small as desired. The cord must be untied to apply the clamp to a vessel and an end unthreaded from the short limb of the T then drawn around the vessel, rethreaded in the instrument and tied with a square knot to the ratchet. The vessel then may be occluded readily by closure of the loop which needs only one hand. Care must be taken not to close it too tightly; otherwise the vessel wall will be injured. It will be found that only the most gentle pressure is needed even to occlude as large a vessel as the aorta or common iliac artery. Once the clamp is in place, the vessel can be occluded or released readily at a moment's notice. This attribute is of the greatest value in the opera-

tion of embolectomy since one has the feeling of complete complacency in being able to control the arterial blood flow once the embolus has been removed. In addition it permits the absolute control during the suturing of the arteriotomy wound. It is readily removed by cutting the cotton cord.

The use of this clamp has made it possible to devise a new and more simple type of embolectomy for a rider embolus at the bifurcation of the aorta (Fig. 1). The advantage of this method is that it is unnecessary to dissect the aorta free in order to control the arterial blood flow. This eliminates the danger of injury to this large vessel which might be catastrophic. The anesthesia of choice in good risk patients is spinal since this gives such complete relaxation of the abdominal muscles. In the poor risk patient ether anesthesia, administered through an endotracheal tube is preferable.

TECHNIQUE OF AORTIC EMBOLECTOMY

The bifurcation of the aorta may be exposed either transperitoneally or extraperitoneally through a right paramedian abdominal incision and the rectus muscle retracted laterally. Murray has recommended the extraperitoneal approach, but in the case reported the transperitoneal method was used. The chief advantage of the latter is that it gives a more direct approach with less retroperitoneal dissection. The extraperitoneal exposure is preferable in obese patients because retraction of the intestines and exposure of the large arteries is more readily obtained. The incision should commence about 2 inches above the umbilicus and extend down to the pubis. If the transperitoneal approach is used the intestines are carefully displaced upward and held with large moist gauze packs. The common iliac arteries and the bifurcation of the aorta are exposed by incising the peritoneum in a triangular fashion over these vessels so that a flap of it can be turned downward. The right ureter should be visualized to avoid damage to it, but it is unnecessary to isolate it. The next step is carefully to free up the right common iliac artery just proximal to its bifurcation. A Bethune clamp is applied at this point and the artery is immediately

occluded. Then the left common iliac artery is isolated. A second tourniquet is applied and the artery occluded just distal to the portion of the embolus which extends into its lumen. With both the right and the left common iliac arteries occluded in this manner the embolus is trapped so that if dislodged there is no danger that it will escape to lodge more distal in the arterial tree (Fig. 1).

The next step is to apply a third tourniquet around the proximal end of the right common iliac artery as near the aortic bifurcation as possible. This clamp is left open but arranged so that it can be closed immediately after removal of the embolus. After the iliac arteries have been controlled in this manner the adventitia is carefully dissected from the mid portion of the anterior surface of the right common iliac artery. A 1.0 to 1.5 centimeter longitudinal incision is made through the vessel wall in this area. The length of it should be no greater than the diameter of the artery. The bifurcation of the aorta is then gently manipulated with the fingers to dislodge the embolus (Fig. 2). Since the left common iliac artery has been occluded just distal to the embolus the arterial pressure forces it into the right common iliac artery. The embolus is rapidly extruded by the tremendous force of the blood. It is not necessary to extract the thrombus by instrumentation within the arterial lumen. If it becomes stuck in the arteriotomy wound gentle squeezing of the artery from above down will aid in its extrusion. A tremendous gush of blood follows the embolus, which is immediately controlled by closing the tourniquet proximal to the arteriotomy wound. This hemorrhage may be terrifying even for the experienced surgeon if preliminary adequate control of the artery has not been obtained. With a rubber tubing around the artery extreme force may be necessary to control it and danger of damaging the arterial wall by an overzealous assistant is real. The greatest value of the Bethune tourniquet in embolectomy is in this step of the operation, since by the gentlest of pressure the arterial flow may be completely stopped. The surgeon is able with one hand to dislodge the embolus while with the other on the clamp he can instantaneously close it after extrusion.

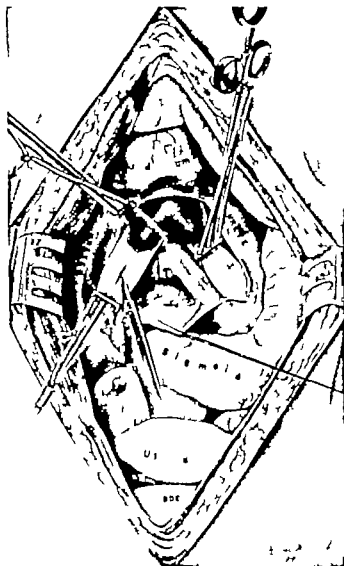


Fig. 1 A drawing to show the technique of transperitoneal aortic embolectomy through a right paramedian incision. The bifurcation of the aorta and the common iliac arteries are exposed by incising and reflecting downward the posterior peritoneum. The method of applying the tourniquet clamps (Bethune type) is shown. They are applied in the following order: the first one is placed on the right common iliac artery just proximal to its bifurcation, the second one the left common iliac artery at the distal end of the embolus and the third one on the right common iliac artery at its origin. The first two clamps are closed while the third remains open until the embolus has been extruded then it is closed. The arteriotomy is between the two clamps on the right common iliac artery.

of the embolus. He therefore has the situation under control at all times.

After the main thrombus has been extruded the left common iliac artery and the bifurcation of the aorta should be carefully palpated for additional clots. The proximal clamp on the right common iliac artery should be released to allow blood to escape and carry with

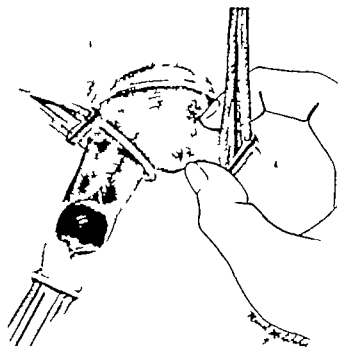


Fig. 2 The method of digital mobilization of the embolus and its extrusion through the arteriotomy in the right common iliac artery.

it any clot remnants to make certain none remain. The clamp is again closed after it is ascertained that there is an active pulsating flow of arterial blood. Every effort should be made to obtain this; otherwise it is certain that occluding thrombi are still present. Then the distal clamp on the same artery is opened with the proximal one closed. Free bleeding should result indicating that the collateral channels and the bifurcation of the common iliac artery are free of thrombi. If active arterial bleeding does not occur exploration should be carried out to remove any fragments of the original embolus lodged in this location. The patency of the left common iliac artery should be tested by releasing the tourniquet on it. If pulsations are demonstrable in the external iliac artery this is sufficient evidence that the left common iliac is patent. If not present it means that another embolus is occluding the bifurcation of the latter and an embolectomy must be performed at this site to restore the circulation of the left lower extremity. These secondary emboli rarely occur but they should be looked for and removed if present. When it is ascertained that there is free bleeding from above and below the arteriotomy incision is closed.

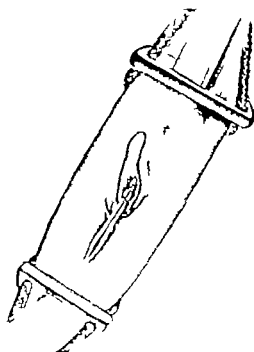


Fig. 3. The mattress closure of the arteriotomy is shown with centrally placed single everting type of mattress suture and continuous hemostatic suture of fine silk.

At this stage in the operation the use of the tourniquet is advantageous in that complete control of the vessels proximal and distal to the incision is obtained so that the edges of the wound are not obscured by escaping blood. Hemostasis is also so effective that little if any blood will be trapped to form a secondary thrombus in the occluded segment of the right common iliac artery during the closure of the arteriotomy wound. As a safeguard in case a small amount of blood may be present 500 units of heparin in a few cubic centimeters of normal saline are placed in the vessel lumen as has also been recommended by Murray. The incision is closed as previously described with a fine nonabsorbable suture. The placing of a mattress suture through all layers of the vessel wall is a useful step to evert the wound edges and permit intima-to-intima closure with a continuous suture.

The tourniquets are removed after the incision is closed. The order in which this should be done is, first, the distal tourniquet on the right iliac artery then the one on the left iliac artery and last the proximal one on the

right iliac artery. The incision in the posterior peritoneum is closed carefully with a running suture of No. 0000 chromic catgut. The abdominal wound is closed in layers without drainage. Heparin is administered by a continuous intravenous drip for 24 hours following embolectomy. If the circulation has been restored as evidenced by a return of pulsations in the peripheral arteries. This is an additional safeguard against secondary thrombosis at the arteriotomy incision. If the circulation has not been restored completely the heparin should be continued for a longer period. A clotting time of 20 to 30 minutes should be maintained during the period of heparinization.

CASE REPORT

M. E. S. N. 77845 a white single female stenographer aged 30 years was admitted to the Baker Memorial division of the Massachusetts General Hospital October 19, 1942 for treatment of pneumonia of 1 week duration. This was her 4th hospital admission. The first 3 were at the Massachusetts Eye and Ear Infirmary for treatment of toxic amblyopia in September and October 1937. The 3d admission was on December 26, 1940, for the

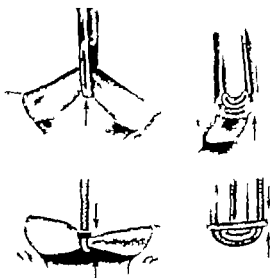


Fig. 4. Drawings to compare arterial occlusion by means of traction on rubber tube (upper left) and by tourniquet clamp (lower left). The arrows indicate the direction of the force applied. Note the angulation of the vessel necessary for occlusion with the tubing, indicating the application of considerable force; whereas closure with the clamp requires relatively small force without disturbing the artery.



Fig. 5 a Drawing of a Cline arterial clamp. The screw control permits too great a mechanical advantage so the force applied to the arterial wall may damage it. b Drawing of a "bull-dog" clamp. The disadvantage of it is that it tends to slip off the artery.

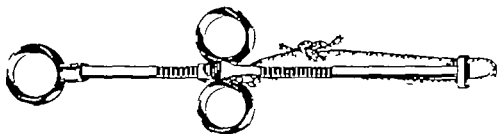


Fig. 6 Drawing of a Bethune type of tourniquet clamp. Its advantages are ease of application, readiness of closure and the small amount of force necessary to occlude an artery preventing damage of its walls.

treatment of bronchopneumonia, rheumatic heart disease with mitral stenosis and auricular fibrillation. She was discharged improved on January 11, 1941.

At the age of 1 year she had had inflammatory rheumatism, at 16 years a streptococcus infection of the throat and at 18 chorea. A diagnosis of inactive rheumatic heart disease with mitral stenosis and insufficiency with cardiac hypertrophy was made in October 1937. There was no evidence of cardiac failure. The remainder of her past history is irrelevant.

Physical examination showed a moderately well developed and nourished woman lying in bed. The general physical examination was negative except for her lungs and heart. Over the right lower lung field posteriorly there were noted decreased resonance, diminished breath sound and increased tactile fremitus and some low rales. The remainder of the lung field was clear. Examination of the heart showed a regular rate of 120 per minute. The first sound at the apex was marked by a systolic murmur and a low pitched late diastolic murmur with crescendo. There was apical diastolic thrill, a systolic murmur was heard at the 3rd left inter space without a thrill. The blood pressure was 110/85. A diagnosis of inactive rheumatic heart disease with mitral stenosis and insufficiency, cardiac hypertrophy and pneumonia in the right posterior lobe was made. The white blood count was 15,100/86 per cent polymorphonuclear leukocytes. The urinalysis specific gravity of 1.01 and was negative for albumin and sugar. The patient temperature was 101 degrees Fahrenheit.

After admission the patient was placed on oral sulfaziazine treatment. She made a satisfactory response to this and was making a normal convalescence until 10:30 p.m. on October 25. At this time while the patient was walking to her bed from

the bathroom, he suddenly felt numbness in both feet. In bed she noticed that her heart began to pound, the numbness became more marked and extended upward and became very uncomfortable with tingling in her leg. At this time her heart rate was 111, grossly irregular. Examination of her feet showed they were cold and there were no arterial pulsation felt in either leg including the femoral arteries in the groin. A diagnosis of a rider embolus at the bifurcation of the aorta was made. The absence of pulsations in her legs was confirmed by oscillometry which showed no oscillation in either extremity.

At 1:30 a.m. (October 6) 3 hours after the time of embolism an operation was performed according to the technique described and an embolus obstructing the bifurcation of the aorta was removed (Fig. 7). Spinal anesthesia was employed 16 milligram of pontocain crystal being used. Following the re-



Fig. 7 The embolus removed from the bifurcation of the aorta. The case that presented.

removal of the embolus there was an immediate return of the arterial circulation as evidenced by pulsations in both feet. Intravenous heparin was given for 24 hours following the operation, and the coagulation time of the blood was maintained at 25 minutes.

Following the operation the patient made a very uneventful convalescence and was discharged from the hospital November 6, 6 days after the embolectomy. A follow up on the patient 6 months after the operation still showed excellent circulation in her legs with pulsations in the right and left dorsalis pedis and posterior tibial arteries.

CONCLUSIONS

The success of an embolectomy depends on (1) early operation (2) direct and adequate exposure of the site of embolism (3) occlusion of the artery distal to the embolus before the artery is disturbed at or proximal to the site of embolism (4) avoidance of damage to the intima, (5) complete control of the arterial inflow both proximal and distal to the arteriotomy so that (6) a meticulous intima-to-intima closure may be accomplished.

The removal of a saddle embolus at the bifurcation of the aorta is a feasible operation if these principles are followed.

The technique of the operation has been simplified by the use of the tourniquet type of clamp for control of the arteries during the embolectomy.

A saddle embolus at the bifurcation of the aorta may be removed readily through an arteriotomy of the right common iliac artery with two clamps on this blood vessel and one on the left common iliac artery without the necessity of freeing up the aorta.

Embolectomy is more readily accomplished by direct exposure of the site of embolism. For this reason a transperitoneal or extraperitoneal approach through a right paramedian incision is recommended for the exposure of the bifurcation of the aorta and the common iliac arteries.

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FURTHER STUDIES ON THE DIAGNOSIS OF BONE TUMORS BY ASPIRATION BIOPSY

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THE first report from Memorial Hospital on the diagnosis of bone tumors by aspiration biopsy was made in 1931 by Coley Sharp and Ellis. Their study was based on 35 cases at a time when this method was in an experimental stage. In all but 1 case tissue was obtained and the operative diagnosis in all but 2 cases proved correct. Three years later (1934) Martin and Ellis (4) made a more exhaustive study of the use of aspiration biopsy at which time 1400 tumors of all types including 140 bone lesions had been aspirated. Coley (2) in the same year in a discussion of Bloodgood's paper on biopsy of bone tabulated 100 cases of bone aspirations in 75 of which the diagnosis had been established. In the remaining 25 there were 3 false positives i.e. a diagnosis of malignant tumor was made but there were errors in the type of cell reported in 22 either no tissue or insufficient material for diagnosis was obtained.

Aspiration biopsy of tumors of bone has now become an established routine in the Bone Tumor Department of Memorial Hospital and we feel therefore that a more recent analysis of results of this procedure is justified. This study includes 567 aspirations of 474 individuals done in the last 12 years in which charts and reasonable follow up are available. The head and jaw regions are not included. Repeat aspirations were necessary for various reasons: failure of the first aspiration; confirmation of the first aspiration or for additional information; multiple or recurrent involvement of bones or as a follow up on treatment.

In this series it should be borne in mind that not all patients with bone lesions seen at Memorial Hospital have had aspiration biopsy; hence the figures given represent only a fraction of all the cases seen in the Bone

Tumor Department. Many enter with the diagnosis already established at other institutions. Others in which it is felt that aspiration cannot yield diagnostic material or in which surgery is elected as the method of treatment are immediately subjected to operation. Tumors of the head and jaw region are not included although several of these cases had the diagnosis established by aspiration of the skull. The aspirations have been done by many different operators; some of them inexperienced so that failure to obtain tissue may have been the fault of the individual and not of the method. Practically every bone of the trunk and extremities has been the site of aspiration as shown by the following tabulation: femur 146, pelvis 111, ribs 72, humerus 52, scapula 37, tibia 40, sternum and clavicle 33, vertebrae 24, fibula 21, small bones 12, radius 11, ulna 8.

Cases have been classified according to the clinician's final diagnosis based on clinical course, x-ray examination, operation, aspiration biopsy and in some cases autopsy findings. Where there was doubt as to the exact type of tumor the case was placed in a separate miscellaneous group. A number of bone lesions not considered bone tumors are seen at Memorial Hospital and must be differentiated from tumor. Some of these are suitable for aspiration though tissue obtained is frequently not satisfactory for diagnosis. It is in the field of true neoplasms that aspiration proves most valuable.

The advantages of aspiration biopsy have been frequently emphasized and will be reviewed here only briefly. It is a simple, rapid, economical procedure. It may clear up a questionable diagnosis or provide histological material in an obvious case without the need for hospitalization and preliminary operation. In many instances it provides microscopic proof for inoperable cases. While an open biopsy

From the Bone Tumor Department, Memorial Hospital, New York.

TABLE I.—ASPIRATION BIOPSY OF BONE LESIONS

Diagnosis	Total cases	Aspiration diagnosis	Tissue obtained but not specific	No tissue by aspiration	Malignant called benign	Benign called malignant	Aspiration procedure at	Repeat aspiration
Osteogenic sarcoma (all histologic types)		67	1				20	27
Endothelial myeloma (2 cases)	22	20		22			5	6
Myeloma (plasma cell and other)	32	27		20				
Giant cell tumor	30			26				
Reticulum cell sarcoma								
Liposarcoma								
Angiosarcoma	1							
Metastatic carcinoma	67	22	6	63				25
Miscellaneous malignant tumors							7	3
Hodgkin disease								
Other (sarcoma, lymphoma, osteosarcoma, chondrosarcoma, fibrosarcoma, giant cell, hemangiosarcoma)								3
Bone cyst								
Paget disease								
Lipoid lesion, cyst				3				
Inflammatory disease		7	16					
Miscellaneous unclassified benign	2						2	
Total		200		300			30	33
Repeat								
Total aspirates	207							

may eventually be necessary no time is lost by aspirating first and it frequently eliminates the more formidable procedure with its attendant hazards of nonhealing and other operative complications.

The foremost disadvantage of this method of diagnosis is the difficulty of interpretation. The pathologist is called upon to make a diagnosis from a minute bit of tissue or from isolated cells and this requires unusual skill and experience. The late Dr. James Ewing, Dr. Fred Stewart, and Dr. Frank Foote of the department of pathology have made careful studies of all material submitted, and it is largely because of their co-operation and skillful interpretation that the value of this method of diagnosis has become established. Stewart emphasizes that the clinical setting, the site of aspiration, the normal cells of this region, and the possible tumors occurring in this location all must be known in order to be able to recognize and interpret the abnormal cells. It is not the aim of the pathologist to classify

the tumor precisely in every case but rather to state whether or not it is malignant and whether or not it is a primary or metastatic tumor. In the present series we have regarded the aspiration as successful if a diagnosis of malignant tumor has been returned. However in many instances especially when a clot for section has been obtained exact type diagnosis has been made. In inflammatory diseases if pus was obtained and other findings are consistent with a benign process the aspiration was also considered satisfactory.

It may be argued that the aspiration may implant tumor cells in the path of the needle, that it may produce hemorrhage in the tumor or loosen cells into the blood stream, thus producing metastases. In no case have we noted any immediate untoward effects. We have not seen development of tumor at or about the site of the needle puncture which would indicate that implantation of tumor cells had occurred along the tract nor has there been any evidence that metastasis was produced or has-

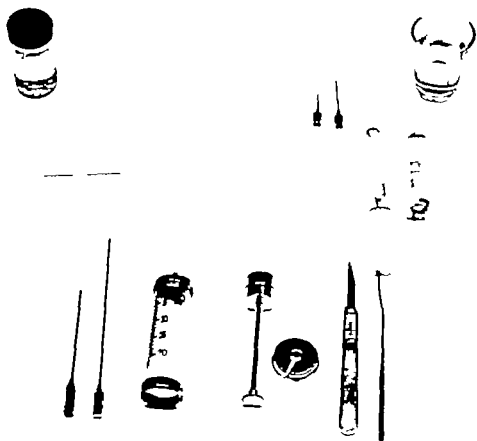


Fig 1. Aspiration biopsy set

tened by the aspiration in any case in which distant disease later developed. In support of this we cite the results of a study of the cases of osteogenic sarcoma seen during the 5 year period from 1932 through 1936. Of a total of 118 cases 62 were aspirated and 56 were not. Nine of those aspirated have survived for 5 years or more without evidence of disease (survival rate of 14.5 per cent). Eight of those not aspirated survived for 5 years or more (survival rate of 14.3 per cent). In this series at least it would seem that there is no evidence that aspiration had been a detriment to survival in a disease which at best has a poor prognosis.

TECHNIQUE

Since the method of obtaining and preparing the material has been fully described by Martin and Ellis (5) we will review it only briefly. Occasionally in infants young children or highly apprehensive adults a short gas anesthesia or intravenous sodium pentothal is used. Fluoroscopic guidance is some times necessary when the lesion is poorly ac-

cessible or when it is in the neighborhood of important anatomical structures. Blady has described the technique for aspiration biopsy in difficult locations. The approach is determined by the roentgenographic appearance. The site should be carefully chosen and usually should be at a point where there is a break in the continuity of the cortex or where there is extension of the tumor into soft tissues. Failure to obtain cells occurs most frequently in sclerosing or intramedullary lesions.

The instruments needed are illustrated in Figure 1. A 20 cubic centimeter record syringe tightly fitted with an 18 gauge needle from 5 to 12 centimeters long is used. The skin is prepared with iodine and alcohol and a small area infiltrated with 1 per cent novocain. A stab wound is made through the skin with a bistoury pointed scalpel (No. 11 Bard Parker blade). The needle is inserted and advanced slowly to the site of the lesion. It can be felt to enter tumor tissue when there is soft tissue extension. In other cases increased pressure must be exerted to puncture the cortex of the

of these were positive. One case was called chondrosarcoma of the distal end of the fibula but its roentgen appearance was that of a benign tumor and local resection showed chondromyxoma only. This is the only instance of a definite false positive i.e. where a benign tumor was called malignant. This is highly significant and important for it means that a report of a malignant tumor can be relied upon at this hospital. It is also well recognized by the clinicians that failure to obtain tissue or material that is diagnostic does not mean that the lesion is not malignant unless all other factors are taken into consideration.

Bone cysts. Cysts are unsatisfactory for aspiration and this procedure is usually not carried out. Seven cysts were aspirated without positive findings except that fluid was obtained in a few instances.

Osteitis deformans. This group is also not satisfactory for aspiration and the procedure is not recommended. One of 6 cases of Paget's disease aspirated yielded material consistent with this diagnosis.

Lipoid histiocytosis. Diseases of this type are occasionally seen and must be differentiated from tumor. One case of Hand Schuller Christian's disease and one of Nieman Pick's with bone changes had the diagnosis established by aspiration. One case of eosinophilic granuloma was called questionably as myeloma and a second case was not diagnostic.

Inflammatory disease of bone. Forty five patients with inflammatory disease of bone were aspirated, the diagnosis being based on a negative aspiration plus an open biopsy in some cases, the roentgenographic appearance, clinical course and history. In 16 cases pus or granulations was obtained and in 7 of 8 cases of tuberculosis the diagnosis was proved by aspiration. The aspiration was of value from a 'negative standpoint. In none of these was a false positive reported.

Miscellaneous benign lesions of bone. There remain 18 cases in which no definite diagnosis was ever established or the condition classified but which were considered benign from their clinical course and other data. No tissue was obtained in any of these.

CONCLUSIONS

The results of 567 aspiration biopsies of bone on 474 individuals have been studied and reported and are summarized in the table. There have been no immediate complications of the procedure and no evidence to suggest more rapid development of metastasis by the use of aspiration to establish diagnosis. In primary bone tumors and metastatic carcinoma of bone 385 cases have been aspirated, of which 67.5 per cent were definitely and specifically diagnostic while a total of 83 per cent showed material sufficient for the diagnosis of tumor, the exact type diagnosis not being called in 14.5 per cent. In only one instance was a diagnosis of malignant tumor made when the resected specimen showed a benign tumor and in this case the treatment was local resection. Thus in no case did a false aspiration diagnosis lead to amputation for a benign process. The clinician must understand the scope and limitations of the method and realize that failure to obtain cells means only that no tissue was obtained further interpretation depending on the clinical and roentgenographic findings. At Memorial Hospital aspiration biopsy has proved itself to be a valuable and reliable diagnostic procedure.

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INTRAVENOUS ALCOHOL IN THE SURGICAL PATIENT

A Preliminary Report

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ALCOHOL in its various forms has been a part of the medical profession's armamentarium since medieval times. Its use as a stimulant, analgesic, and anesthetic is well known. In 1929 Marin wrote his doctoral thesis on the subject of Intravenous Anesthesia with Ethyl Alcohol (1) The popularity of this method however was curtailed because its users reported such complications as hemolysis, sclerosis of the blood vessels, shock and decreased urinary output. In 1939 Mueller reviewed a series of 2,000 cases in which 5 per cent and 10 per cent alcohol solutions were infused. Since this paper, a new interest has developed in intravenous alcohol from the analgesic and caloric standpoint. Dr Vincent O Conor has utilized 5 per cent alcohol for his operative cases since June of 1941. His excellent results with this method have stimulated our interests and have led us to expand its use to other surgical specialties. This report is based on an analysis of the last 150 cases.

The physiological effects of alcohol have been thoroughly investigated by many scientific workers (5 8) When 1000 cubic centimeters to 3000 cubic centimeters of 5 per cent or 10 per cent alcohol in 5 per cent glucose is administered intravenously over a 24 hour period the patient experiences a dulling of memory and concentration. He has a sense of well being and loss of anxiety. Respirations are increased (6) the blood pressure shows no significant change, the pulse may increase slightly there is a vasodilatation but the body temperature remains the same or decreases slightly. Alcohol does not have any bronchoconstrictor action and seldom any bronchodilator action as shown from determination of the dead space of breathing (6) Nausea and vomiting, acidosis, and headache are not concomitant symptoms when the alcohol is used intravenously; they do occur however when it is taken orally in comparable doses (3 10 12). There is an increase in the flow of urine which is due to the fluid intake not to the diuretic effect of the alcohol alone. Ninety to ninety nine per cent

of the alcohol is completely oxidized in the body. Approximately 2 per cent is excreted in the urine and from 0.2 per cent to 0.5 per cent is eliminated by the lungs. In our series of cases blood analyses have shown 0.2 milligram to 1.0 milligram alcohol per cubic centimeter of blood immediately after and during the course of administration. If the blood concentration of alcohol is above 0.5 to 0.7 milligram, the patient shows signs of inebriation (5 9). The amount in the blood varies with the rate of infusion, metabolic rate and tolerance of the patient (7). The official U S Navy test has been used in our determinations. The details of the test are as follows:

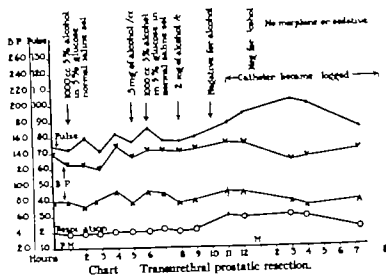
NAVY TEST

1. Take 2 c.c. of whole blood, plasma, or serum.
2. Add 15 c.c. of picric tartaric reagent. Picric-tartaric reagent—one half saturated picric acid containing about 10% tartaric acid.
3. Distill and collect the first 10 c.c. of distillate.
4. Take 3 clean test tubes.
5. Add 1 c.c. of distillate to tube No. 1.
6. Add $\frac{1}{2}$ c.c. of distillate plus $\frac{1}{4}$ c.c. of distilled water to tube No. 2.
7. Add $\frac{1}{2}$ c.c. of distillate plus $\frac{1}{4}$ c.c. of distilled water to tube No. 3.
8. Add 1 c.c. of $N/5$ $K_2Cr_2O_7$ in 50 per cent H_2SO_4 .
9. Place in a boiling water bath for 10 minutes.
10. Compare color of each tube with those of the standard using the colorimeter.

The normal individual metabolizes approximately 10 cubic centimeters of pure alcohol per hour (8 11). This rate is a constant one regardless of the concentration in the blood. If this level is exceeded intoxication may occur. This basic fact must be kept in mind when the drug is administered. A 5 per cent alcoholic solution therefore will contain 10 cubic centimeters of 95 per cent alcohol per 200 cubic centimeters of fluid. In 1 hour this amount will be entirely metabolized in the average individual. Cautious additional amounts above this figure will give the milder forms of euphoria and intoxication which are needed for clinical results, as these vary with the individual tolerance. Therefore it is best to judge the rate of infusion by the subjective signs.

The clinical uses of intravenous alcohol are mirrored through its many physiological effects. It has a special value in those cases in which nausea, vomiting, and paralytic ileus prevail (2 3 10 11).

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These patients are starving. It is a known fact that a person in a normal state of health can support himself from his own body surpluses for 3 to 4 days without serious damage to his protein, carbohydrate and fat stores. However beyond this limit, the body starts to draw from its reserves. One thousand cubic centimeters of 5 per cent glucose in normal saline will provide 200 calories. With the addition of 50 cubic centimeters of 95 per cent alcohol the caloric intake is increased to approximately 600 calories (3, 12). Thus, a solution of 5 per cent alcohol and 5 per cent glucose in physiological saline tends to protect the body proteins, carbohydrates, and fats, because it is a utilizable source of energy which is not stored. Vitamins may be added to the

alcohol solution without rendering the vitamins inactive (10).

The sedative and analgesic qualities of the 5 per cent alcohol solutions are very dramatic (4, 10). With spinal anesthesia, which is used in 22.2 per cent of our urological surgical cases, we have employed 5 per cent alcohol as a supplement during the entire operative procedure. Patients who have this form of medication, do not relax, lose all apprehension and often have no memory of the surgical interlude. Postoperatively the 5 per cent alcohol solution has been continued with the most gratifying results. The use of an opiate or other sedative may be eliminated entirely if the rate of flow of the intravenous alcohol is regulated to the patient's needs. We do not permit more than 3000 cubic centimeters of the 5 per cent alcohol over a 24 hour period. We usually find 1000 to 2000 cubic centimeters adequate.

The value of intravenous alcohol in postoperative recovery is twofold. Not only is it given as a sedative and analgesic, but as a safeguard against the possibility of atelectasis and other pulmonary complications. The respiratory rate and tidal exchange remain the same or are increased (5, 6).

The vasodilatory effects of alcohol suggested its use in the cardiac patient (5, 13). In 5 per cent and 10 per cent solutions, it is beneficial in patients troubled with heart diseases. It increases the dilatation of the blood vessels and possibly the coronary arteries, so that even though fluids are given intravenously the blood pressure is not significantly increased. In cardiacs, one may use a 10 per cent solution of alcohol thereby decreasing the actual amount of fluid intake necessary to maintain the required caloric intake.

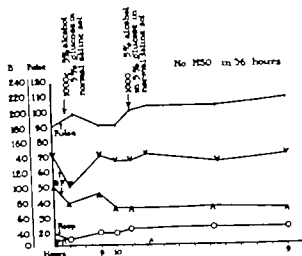


Chart Abdominoepidural operation—500 cubic centimeters of 5 per cent alcohol in glucose during surgery

In the debilitated and morbid patient we have eased restlessness and pain. In the cancer patient who has previously been made comfortable with fluids and morphine we have markedly reduced the necessity for opiates. In the alcoholic who is approaching or has developed delirium tremens due in part to the sudden withdrawal of his customary alcoholic intake we have been successful in controlling him with intravenous alcohol when all other medications in the usual dosages have failed.

The complications that have occurred from the intravenous infusion of 5 per cent or 10 per cent alcohol have been minor. Occasionally when the fluid had been given too rapidly there has occurred restlessness and inebriation. It is singular that few cases have needed restraint. The infusion can be discontinued or slowed with the resultant return to the quiet state of well being. Occasionally the administration has been complicated by the sclerosed vessel. This occurs more frequently with the 10 per cent than the 5 per cent solution. We have had one partial ulnar nerve paralysis which may have been caused by subcutaneous alcohol in the cubital fossa. Because of this occurrence we suggest the use of blood vessels other than those in the cubital fossa and recommend that the beginner at venipuncture use saline for the cannulation of the needle before changing to alcohol. In numerous cases the alcohol has run subcutaneously without causing symptoms other than slight discomfort. This has been relieved by warm, moist applications.

SUMMARY

1. Five per cent and 10 per cent alcohol intravenously increases the caloric intake and has special value in those cases with inanition.

2. It is a potent sedative and analgesic, and can be substituted for the opiates and other forms of sedation.

3. Sedation is not attended with depressed respiration.

4. It may be used in cardiac patients with relative safety because of its vasodilatory effect and minimal effect on the blood pressure.

5. It has a definite place in regional anesthesia as a supplement during the operative procedure.

6. It has proved its value in alcoholic patients who cannot be controlled with the usual doses of narcotics.

7. At the present we have found no contraindications.

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THE INFLUENCE OF THYROIDECTOMY ON THE PROMINENCE OF THE EYES IN THE GUINEA PIG AND IN MAN

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ONE of the most perplexing problems in the field of physiology of the thyroid gland is the relationship of exophthalmos to thyroid disease. Why an occasional patient with exophthalmic goiter experiences an increase in exophthalmos after thyroidectomy while the great majority of patients appear to have been benefited presents a question.

Careful study has been made of the changes in prominence of the eyes of experimental animals and of patients after thyroidectomy. With regard to patients, efforts have been made to discover the relationships between the clinical features of thyroid disease and the demonstrable changes in the eyes after thyroidectomy. The studies of guinea pigs evolved from other experimental studies in which it was found that it was impossible to establish a definite, constant eye reading with regard to prominence of the eyes in guinea pigs after thyroidectomy. The eyes seemed to be increasing in prominence.

ANIMAL EXPERIMENTATION

A review of the literature revealed a difference in opinion regarding the effect of thyroidectomy on prominence of the eyes of experimental animals. Some investigators have reported a noticeable increase in prominence in different species (8-18). Others failed to find this change (1-7). It has been shown that proptosis in guinea pigs is produced more easily with thyrotropic hormone after thyroidectomy has been performed than in guinea pigs that have not been thyroidectomized (1-7, 13). Furthermore one investigator (7) has demonstrated that proptosis, similarly produced in guinea pigs that have not been subjected to the thyroidectomy, does not become apparent until the animals have become refractory to the

thyrotropic preparation and their basal metabolic rates have begun to decline. Finally it has been shown that proptosis can be produced with methyl cyanide much more easily after thyroidectomy (17-18) than if thyroidectomy has not been performed.

Probably the best explanation for the differences in opinion regarding the effect of thyroidectomy on the prominence of the eyes of experimental animals is that investigators had no very reliable means of measuring exophthalmos. The earliest methods consisted of studying animals in pairs and comparing their gross appearances (11-18). More recently measuring devices placed on the head and even on the corneal surface have been used (20-25). A camera lucida (1-3) method has been used to avoid touching the cornea. In these methods, however, rather vigorous restraints were required a fact which may contribute to error. The necessity for more accurate methods of measuring proptosis in animals becomes apparent.

EXPERIMENTAL METHODS

Two improved methods, about equally accurate, have been devised for measuring exophthalmos in guinea pigs. In the first method callipers were used to measure the intercorneal distance. An animal was placed beneath the frame (Fig. 1) and, by sighting through the peep-sights above the animal's head the blades of the callipers could be arranged in line with the corneal surfaces on the two sides without touching the animal. The net distance between the peep-sights depended on the average size of the heads of the group of guinea pigs to be studied.

The second method involved the use of the camera lucida (Fig. 2). The guinea pig was placed in a trough equipped with a sliding floor which could be moved forward until the head of the animal was a given distance from the camera lucida. This distance was determined by a fixed rod (Fig. 2 d). By looking through the aperture of the camera lucida the image of the animal's head could be seen on a plane which carried a sliding scale (Fig. 2 e). The scale was so arranged

From the Division of Surgery, M. S. Foundation.
Abstradgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

The experimental work was done in the laboratory of Dr. George M. Haggard, at the Institute of Experimental Medicine; the clinical work under the guidance of Dr. Samuel F. Hildner. Presented before the Society for the Study of Internal Secretions, Chicago, June 8, 1944.

that 10 centimeters at the position of the animal's head was equal to 10 centimeters on the sliding scale. Thus, the intercorneal distance could be measured without touching the animal.

It was found that if the animals were placed in the dark for 20 minutes preceding the measuring procedure and then were exposed to the bright light associated with the measuring device, many of them froze into a rigid position. This state, when acquired, eliminated the necessity of forced restraint and greatly reduced the errors incident to measuring the degree or extent of proptosis.

Because these methods proved essentially equal in accuracy, both were used in the experiments which form the basis of this report. Measurements were obtained on each animal three times with each method each day they were observed. The average of these six determinations was accepted as the status of the prominence of the eyes for that particular day. The accuracy of these methods was tested by study of several normal guinea pigs, the water balance and salt intake of which were modified. Comparatively slight changes in body weight, due to hydration, were accompanied by parallel changes in prominence of the eyes (Fig. 3).

EXPERIMENTAL PROCEDURE AND RESULTS

With these methods of measuring exophthalmos, which were somewhat more accurate than

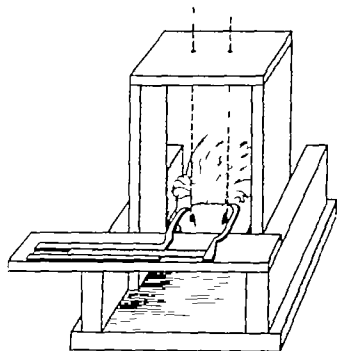


Fig. 1. Improved calliper method of measuring intercorneal distance.

methods previously devised, an experiment to determine the effect of thyroidectomy on the prominence of the eyes of guinea pigs was undertaken. Seventeen normal male pigs, weighing from 325 to 500 grams were selected for their susceptibility to the measuring procedure. The

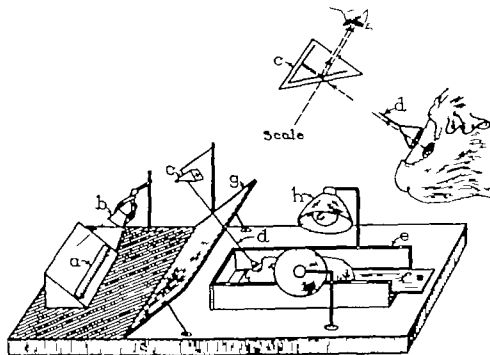


Fig. 2. The camera lucida method of measuring the intercorneal distance. *a* millimeter scale; *b* daylight blue microscope lamp; *c* camera lucida; *d* distance rod, to control distance between camera lucida and head of animal; *e* trough to hold animal; *f* sliding floor; *g* right shield; *h*, lights to illuminate animal.

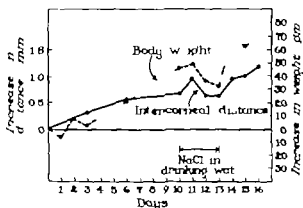


Fig. 3. T illustrate parallelism between changes in body weight and prominence of the eyes of a growing, normal animal.

teen were thyroidectomized and 4 served as normal controls. The prominence of the eyes was measured preoperatively and postoperatively at intervals of 1 to 4 days. Changes in body weight also were determined.

The results of the experiment are illustrated (Fig. 4). It was found that although the thyroidectomized animals failed to increase in body weight, prominence of the eyes did increase. This increase in proptosis was out of proportion to the slight increase which was demonstrated by the normal animals that had gained much more weight.

Thus it can be seen (Fig. 5) that it is important to determine the increase in width that takes place in that portion of the skull which lies between the orbits. The supraorbital notches of the guinea pig's skull lie above the medial boundaries of the orbits. Fortunately, these notches are just beneath the skin and thus are easily located with the blades of appropriate callipers. It is therefore possible to measure the distance between the supraorbital notches in exactly the same way as several successive occasions. Changes in distance between the supraorbital notches (a in Fig. 6) must be deducted from the change in intercorneal distance (b) in order to obtain a true evaluation of the proptosis. The determination in this way of the changes in width of that portion of the skull which lies between the orbits served as a control.

In the lower right portion of Figure 4, measurements of the frontal bones made by this method are illustrated. In the thyroidectomized animals, there was not much increase in width of that portion of the skull which lies between the orbits; this is in keeping with the slight changes in body weight of these animals. On the other hand, in the normally growing controls, there was somewhat more increase in this measurement of the skull. When these skull measurements are deducted from the changes in the intercorneal distance, emphasis is added to the already established fact that thyroidectomy results in increase in prominence of the eyes.

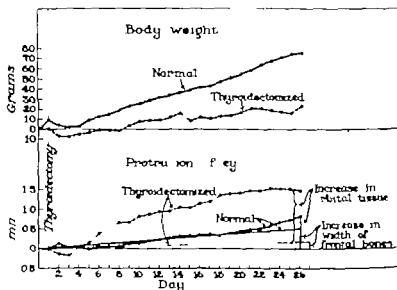


Fig. 4. Changes in the prominence of the eyes resulting from thyroidectomy performed on the normal guinea pig. The increase in the width of the frontal bones, as illustrated in the lower right portion of the graph, is represented by the same scale as the measurements dealing with the eyes.

TABLE I—CHANGES IN PROMINENCE OF EYES OF PATIENTS WITH EXOPHTHALMIC GOITER OR ADENOMATOUS GOITER FOLLOWING SUB TOTAL THYROIDECTOMY

	Exophthalmic		Adenomatous	
	N	Per cent	N	Per cent
Total cases	98		35	
Decreased or remained the same	2	3	6	4
Increased 5 to 5 mm	3	2.6	30	37
Increased 5 to mm	29	29.6	10	34
Increased mm more	35	35.7	22	24

This increase in proptosis is in all probability due to an increase in the retrobulbar tissues, for it is well recognized that changes in the globe are negligible. Six of the 13 thyroidectomized animals were killed at the conclusion of the experiment. Histologic studies of the tissues revealed minimal edema of the retrobulbar tissues in 3 of the 6 in stances. Smelser (25) has shown by analytical methods that there is a slight increase in the water content of orbital fat of guinea pigs after thyroidectomy.

CLINICAL OBSERVATIONS

The reports in the literature dealing with this problem as it relates to patients disagree. Bartlett (3, 4) in discussion of other papers, declared that prominence of the eyes of patients increased after thyroidectomy, but he failed to present any data to support his contention. Grace and Weeks reported that prominence of the eyes of their

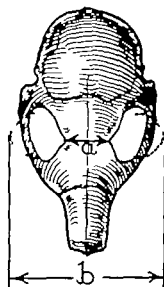


Fig. 5 Skull of guinea pig. a distance between supra-orbital notches b intercorneal distance

series of patients did not increase after thyroidectomy. Their measurements were made with an exophthalmometer. When and how frequently they made measurements is not certain. Solev (26, 27) reported that the prominence of the eyes increased after thyroidectomy for exophthalmic goiter or adenomatous goiter with hyperthyroidism.

The present investigation deals with 233 consecutive patients who underwent thyroidectomy. The Hurler exophthalmometer was used. Measurements were made preoperatively and at intervals of 1 to 4 days postoperatively. The shortest period of observations was 14 days. The exophthalmos was measured six times on each day that

TABLE II.—A TYPICAL RECORD ILLUSTRATING THE INCREASE IN PROMINENCE OF THE EYES FOLLOWING THYROIDECTOMY IN A CASE OF EXOPHTHALMIC GOITER†

Relation to operation, days	Measurements, mm.						Body weight		Basal metabolic rate per cent
	Right eye			Left eye			Pounds	Kg	
6th preoperative									+40
Operation ‡	12	5	5	13.5	3	3	20	34	
2nd postoperative	13.5	3.5	3.5	13.5	3.5	3.5			
5th postoperative	12.5	14.5	4	13.5	3	3.5			
9th postoperative	14	4	14	14	4.5	4	22	33	
21st postoperative	4.8	14.5	4.8	4	14.5	14.5	12.3	26	
16th postoperative	14.5	4.5	4.5	4.5	14	14.5	24	36	+
9th postoperative	5	5	5.5	5	5	5	5	37	
23rd postoperative	8.5	5.5	6	6	5.5	5.5	5	37	

*Thyroidectomy in this case consisted of subtotal resection, leaving in place 1 of each lobe of the thyroid gland. The right inferior thyroid artery was ligated.

†P. Urthoe diagnosed based on the 36 gm. of tissue removed was diffuse parenchymatous hypertrophy.

‡Exophthalmometer setting, 3.

§Readings are made before the operation on this day. The day of operation is counted as the 1st day. Clinic, as the first postoperative day.

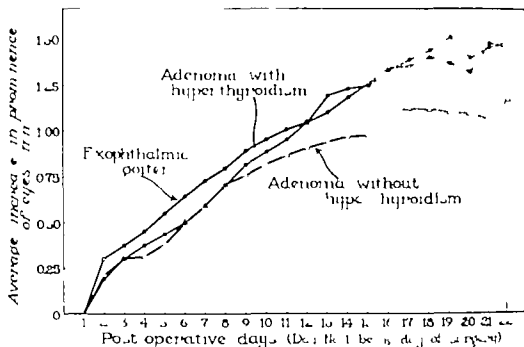


Fig. 5. The average prominence of the eyes after thyroidectomy for three types of goiter. This is the average of the individual graphs made for each patient. At the fifteenth day the average of the patient represented by the solid line should fall. The increase evident by the broken lines. The use of the data of the first week represented to illustrate the dominating rate of change.

observations were made three times in each eye. The average of the three measurements represented the observation for this day. Great care was taken to make the measurement in the same way and under the same conditions at all observation. In the course of the investigation a little more than 10,000 exophthalmometer readings were made and in this large number of readings it seems reasonable to assume that variations in the technique of making the measurements were reduced to a minimum. The importance of making the measurement at the same time after the patient's arising was recognized. Importance also was attached to having the eyes in the same position at each measurement. This was accomplished by having the subject look with the right eye at the observer's right ear and with the left eye at the observer's left ear so that the same point on the cornea was observed each time.

The eyes of all but 9 of the 233 patients, regardless of pathologic state increased in prominence following thyroidectomy. However, the increase in 8 cases, or approximately one third of them, was 1 millimeter or less, which is negligible.

Physiologically exophthalmic goiter and adenomatous goiter are different (19). Therefore it seems reasonable to consider separately the two groups of patients representative of these diseases.

The contribution of the patient according to the different degrees of ocular prominence that developed is given in Table I. It is evident that of the patients whose eyes increased in prominence about one third fell in each of the categories set down in the table. The greatest average increase in prominence of the eyes among the patients with adenomatous goiter was 4 millimeters and, among the patients with exophthalmic goiter it was 3.5 millimeters. A typical record of a patient with exophthalmic goiter is presented in Table II to illustrate the value of the multiple readings mentioned and the gradual change in prominence of the eyes that is demonstrable in this manner.

The course of events with reference to the eyes of each of the 233 patients was plotted individually and the composite of these records is presented in Figure 6. It has been found that prominence of the eyes of the patients who had adenomatous goiter with hyperthyroidism or exophthalmic goiter was more greatly increased after thyroidectomy than was that of patients who had adenomatous goiter without hyperthyroidism. Because of the volume of data on which this report is based this difference is probably significant.

Control observations were made on 16 patients, 8 of whom underwent surgical procedures which

TABLE III — CHANGES IN THE EYES FOLLOWING SURGICAL PROCEDURES OTHER THAN THOSE ON THE THYROID GLAND

Change prominence of eyes			
Decrease from 5 mm	% change to norm	Increase of 5 mm	Inc case of more than 5 mm
cases (1 of 6, abdomen opened)	0 cases (16 of 9, abdomen was opened)	1 case (parathyroid tumor)	cases

were confined to the region of the neck but were not for thyroid disease. The other 8 patients were subjected to procedures which required opening of the abdominal cavity. Among these patients contrary to the findings after surgical operation on the thyroid gland was a group of 6 whose eyes decreased in prominence after the operations (Table III). Five of the 6 were patients whose abdominal cavities were opened and whose fluid balance probably was disturbed after operation. Nine of the 16 patients fell into the group in which prominence of the eyes after operation ranged from no increase up to an average increase of 1 millimeter. That increase has been regarded as negligible. In the 1 case in which the average increase was 1.5 millimeters a parathyroid tumor had been removed. In this case it was necessary to interrupt a considerable part of the blood supply of the thyroid gland and to mobilize both of its lobes in order to discover and remove the parathyroid tumor that was lying posterior to the thyroid.

Since the data suggested that prominence of the eyes increases after thyroidectomy it seemed reasonable to evaluate the increase in terms of the other clinical features of thyroid disease. Since this study suggests that there is a correlation between the change in basal metabolic rate and the change in prominence of the eyes, this and various other correlations will be considered first with reference to exophthalmic goiter.

It was found among the patients with exophthalmic goiter that if the initial basal metabolic rate was relatively high the increase in prominence of the eyes following thyroidectomy was in some cases relatively striking. However although this was statistically significant it was scarcely impressive.

A more significant correlation was found between the change in prominence of the eyes and the fall in the basal metabolic rate which resulted from operation. The cases of exophthalmic goiter were divided into two groups in relation to the magnitude of the postoperative fall in basal metabolic rate, namely those in which the fall

TABLE IV — THE FALL IN THE BASAL METABOLIC RATE AS RELATED TO CHANGES IN PROMINENCE OF THE EYES FOLLOWING OPERATION FOR EXOPHTHALMIC GOITER

	Decrease basal metabolic rate			
	Per cent			
	Less than 5		More than 5	
	N	P	N	P
Increase of 5 mm or less	5	51		
Increase of 5 to 10 mm	8	9	6	28
Increase of 10 mm or more	3	9		4
Total cases	28		7	

was less than 30 per cent and those in which it was more than 30 per cent. The patients whose basal metabolic rates fell slightly were inclined to relatively slight increase in prominence of the eyes whereas those whose basal metabolic rates fell markedly were inclined to relatively great increase in prominence of the eyes (Table IV).

Still considering exophthalmic goiter a study of the relation of preoperative exophthalmos to the postoperative change in prominence of the eyes was made. There was no correlation between presence or absence of preoperative exophthalmos and postoperative increase in prominence of the eyes.

Cognizance was taken of the presence of thyroditis in those cases in which a pathologic diagnosis of parenchymatous hypertrophy of the thyroid gland was made. Thyroditis was recognized as consisting of more than the usual scattering of lymphocytes usually seen in the thyroid gland in cases of exophthalmic goiter. There was no correlation between the presence of thyroditis in association with exophthalmic goiter and change in prominence of the eyes after surgical treatment. It has been recognized in the Mayo Clinic however that in surgical cases of exophthalmic goiter in which extreme degrees of thyroditis exist hypothyroidism is more likely to develop relatively late in the postoperative course than it is in cases in which there is no thyroditis. The presence of thyroditis therefore may be correlated with changes in prominence of the eyes that are found relatively late after operation.

The weight of the thyroid tissue removed in the case of exophthalmic goiter is a relative estimate of the total weight of the gland. The weight of the tissue removed in the cases of exophthalmic goiter was determined and related in the following table.

postoperative changes in the eyes. The data suggest that there is no clear-cut correlation between the weight of the thyroid gland and the increase in prominence of the eyes after operation. The sex of the individual likewise had no relation to the postoperative change in prominence of the eyes in cases of exophthalmic goiter.

Now dealing with exophthalmic goiter, clinical and pathologic features in cases of adenomatous goiter were studied with regard to changes in prominence of the eyes which followed thyroidectomy. Those patients who had a adenomatous goiter associated with hyperthyroidism were more inclined to develop a striking increase in prominence of the eyes after thyroidectomy than were patients who had an adenomatous goiter not associated with hyperthyroidism. The difference in these two types of adenomatous goiter was slight but definite in view of the large number of observations (Fig. 6).

Attempts to estimate the amount of thyroid tissue remaining after removal of adenomas were unsatisfactory.

The presence of intra-adenomatous hypertrophy had no relation either to the changes in prominence of the eyes or to the preoperative basal metabolic rate.

DISCUSSION

It has been demonstrated that there is an increase in prominence of the eyes during the first 3 weeks following subtotal thyroidectomy. This confirms the findings of Soley (26-27). The question arises as to what the outcome of this ocular change may be. Obviously if the increase continued indefinitely at the same rate it long would have been a recognized clinical fact. At the time of writing of this report 14 patients had been seen 2 or more months after thyroidectomy and for the most part the increase in ocular prominence that previously had been demonstrated had not regressed.

Correlation was found between the fall in the basal metabolic rate and the increase in prominence of the eyes in cases of exophthalmic goiter after thyroidectomy. Although comparatively few of the patients were followed subsequent to the period of 3 weeks of observation those who have been followed have given evidence of a similar correlation. Nine out of 10 of those who have been seen several months after surgical treatment and whose basal metabolic rates have fallen even more than at the end of the period of 3 weeks, have demonstrated further increase in prominence of their eyes. It is of further interest that most of such patients who have received thyroid extract have shown a regression in the prominence of the

eyes as the basal metabolic rate has returned to normal. Since the indications are that fall in basal metabolic rate subsequent to the short period of observation covered by most of the study is accompanied by further increase in prominence of the eyes, thyroditis (lymphocytic infiltration of the thyroid) and its predisposition to postoperative hypothyroidism may have some bearing on changes in the eyes.

Thirteen patients who have sought treatment for myxedema either of postoperative or spontaneous origin gave evidence of regression in the prominence of their eyes when thyroid extract was administered to raise their basal metabolic rates. This phenomenon seemed more noticeable among those patients who had suffered from their hyperthyroidism for a relatively short period of time.

To the casual observer almost all of the patients described in this study have seemed to show gross improvement in prominence of their eyes after thyroidectomy. I am impressed by the fact that there is a distinction between actual prominence of the eyes and the other numerous eye signs such as retraction of lids, stare, tension of the muscles of expression and so on which contribute to the exophthalmic appearance. It seems, therefore, that it is improvement in these latter signs which mask the actual increase that takes place in prominence of the eyes after thyroidectomy in exophthalmic goiter.

In accepting the observations on basal metabolic rate in cases of exophthalmic goiter it is important to recognize that many of the patients had been subjected to varying degrees of treatment with iodine before presenting themselves for treatment at the clinic. The initial basal metabolic rate therefore reflected varying degrees of iodination with its accompanying influence on metabolism.

No patient in this series, up to the time of writing of this report had been recognized as presenting progressive postoperative exophthalmos or malignant exophthalmos, which has been the subject of important studies by Naffziger and others. Prominence of the eyes of one patient has increased as much as 4 millimeters but the patient did not appear to be exophthalmic.

SUMMARY

Observations have been made on the changes in the prominence of the eyes after total thyroidectomy performed on 13 guinea pigs and after subtotal thyroidectomy performed on 133 patients. An improved caliper method and a camera lucida method have been devised and found more

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accurate than some previous methods for studying such changes in experimental animals. Multiple readings were made on the animals with these instruments and more than 10,000 exophthalmometer readings were made on patients. Increase in prominence of the eyes of both experimental animals and of patients was found. Among patients there apparently was some correlation in the fall in basal metabolic rate and the increase in the prominence of the eyes. The presence of thyroiditis, the sex of the patient, the weight of the thyroid tissue removed, the presence of intra-adenomatous hyperplasia and the presence of preoperative exophthalmos apparently had little or no correlation with the changes in prominence of the eyes after subtotal thyroidectomy performed on patients.

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TOTAL GASTRECTOMY

Report of Eight Cases

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In the past many patients with extensive gastric lesions have been said to be surgically incurable and thus have been deprived of the benefit of total gastrectomy because of the prohibitive operative mortality. The procedure should be limited to those patients in whom the lesion is too extensive or too close to the esophagus to make subtotal gastrectomy feasible; then it is the only alternative. Refinement of technique and increased operative ability with a resultant decrease in mortality have rendered total gastrectomy practicable in selected cases. Until 1922 the mortality rate in all cases of total gastrectomy reported in the literature was 53.8 per cent according to Finney and Rienhoff. Recently Collier and associates (2) reported only 2 deaths in 10 cases or a mortality of 20 per cent. Our series of 8 consecutive cases was without operative mortality.

The history of total gastrectomy is a remarkably hazy one in the literature by Walters, Finney, and Rienhoff, Rieder, Lahey, and others. Schlatter is generally credited with the first successful total gastrectomy in 1897, his patient living for 1 year and 53 days. Rieder found only 88 authenticated cases reported up to 1913. Since then the increase in reported cases shows a definite trend toward this procedure in selected cases.

INDICATIONS

Total gastrectomy is particularly adaptable for the linitis plastica type of stomach. However, it is also indicated in neoplasms extending into the cardiac end of the stomach and even in deep penetrating ulcers located high in the stomach and therefore not amenable to medical management or to subtotal gastrectomy.

In the 8 consecutive cases of total gastrectomy presented here, operation was performed since March 1943. Three patients had localized ulcerating carcinomas, high in the stomach; in 2 extensive infiltrating neoplasms involved most of the stomach; 2 patients had persistent penetrating benign ulcers high in the cardia; in 1 patient with multiple lymphosarcomatous lesions of the stomach a single tumor was located only 1 inch from the esophageal orifice. Pertinent information concerning these cases is summarized in Table I.

From the Cleveland Clinic.

The symptoms in all cases were unbearable and consisted chiefly of pain, obstructive symptoms, or both. In Cases 4 and 7 chronic intractable ulcers caused acute penetrating pain. Each patient had extensive medical management without relief and welcomed surgical intervention. Operation was undertaken to provide relief from symptoms and to enable the patient to live some months or years of fairly comfortable and productive life.

OPERATIVE TECHNIQUE

Technically total gastrectomy is a most difficult procedure requiring a adequate exposure, mobilization, and some degree of mechanical skill. Experimental work, such as that of Mann (3) who had only 3 survivals in a large group of dogs, substantiates these difficulties. We believe that certain features in the operative technique in our series contributed to the success of the operation and deserve mention.

1. The use of spinal anesthesia in all cases, since it offers ideal operative conditions resulting in the best relaxation and exposure. In addition it enables the patient to co-operate in the immediate postoperative period when forced coughing may abort an incipient atelectasis.

2. The use of an upper midline incision in preference to any other because it enables the surgeon to work to the right or left with equal facility and results in primary healing without herniation.

3. The removal of the stomach, since the esophagojejunostomy anastomosis is thus made easier than when the stomach is left intact and used as a retractor to pull down the esophagus for suture. The use of only two layers of suture for anastomosis—a continuous external layer of medium silk (first applied posteriorly) and a mucosal layer of chromic catgut.

4. The dissection of a shelf of diaphragmatic peritoneum which is resutured to the jejunum below the line of anastomosis and thus acts as a suspensory to relieve the suture line of some stress.

5. The insertion of the loop of jejunum through the transverse mesocolon. This was not possible in 1 patient who had x-ray therapy 3 years before and multiple adhesions prohibited the posterior operation.

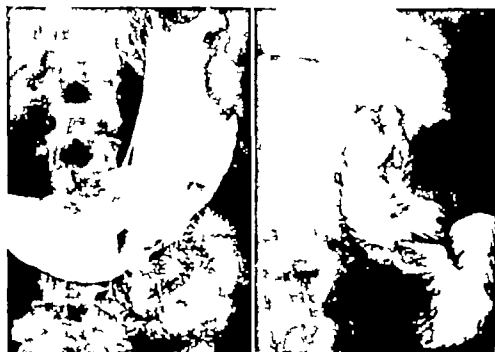


Fig 1. Multiple lymphosarcomatous lesions of the stomach. Postoperative films showing normal esophageal markings with no obstruction to flow of barium. Intestinal loops empty rapidly with normally functioning enteroenterostomy.



Fig 2. Peptic ulcer high in cardia along lesser curvature. Clinical impression was malignant lesion, but microscopic studies proved it to be benign. Postoperative films showing excellent functioning of anastomosis without obstruction.

6 The creation of an enteroenterostomy between the afferent and efferent loops of jejunum in order to allow the pancreatic enzymes and biliary secretions to bypass the esophagus and prevent regurgitation.

7 The closure of the wounds with interrupted steel alloy sutures, which in our experience minimizes wound infections and their undesirable sequelae.

8 The mobilization of the left lobe of the liver

TABLE I.—SUMMARY OF CASES REPORTED

Age	Sex	Preoperative condition	Operation	Postoperative course	Hospital days	Mortality
21	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
22	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
23	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
24	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
25	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
26	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
27	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
28	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
29	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
30	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
31	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
32	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
33	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
34	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
35	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
36	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
37	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
38	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
39	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
40	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
41	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
42	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
43	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
44	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
45	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
46	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
47	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
48	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
49	M	Ulcer	Partial gastrectomy	Unremarkable	10	—
50	M	Ulcer	Partial gastrectomy	Unremarkable	10	—

by division of the lateral ligament has not been found necessary for exposure.

9. Splenectomy as a routine procedure or to increase exposure does not seem justifiable and is not without danger. Vascular accidents are not uncommon after splenectomy. Splenectomy may be indicated in uncontrollable bleeding from trauma. Splenectomy was performed in 1 case because of extension of malignant lesion into the gastrosplenic ligament and perisplenic areolar tissue.

10. The removal of the gastric tube at the completion of the operation in order to prevent pressure necrosis at the line of anastomosis.

Preoperative preparation consists of daily gastric lavage, intravenous saline injections, transfusions when indicated, administration of parenteral vitamins, and a careful determination of renal and cardiac reserve. Gastric lavage is done 2 hours after meals each night. If the gastric residuum is consistently over 100 cubic centimeters, continuous suction is used for 36 hours immediately before operation. Five hundred cubic centimeters of intravenous 3 per cent saline is given each morning until the excretion of urinary chlorides is normal.

After operation only sips of water are given by mouth for 4 or 5 days. Then the patient is gradually started on small amounts of liquid food. In-

take is slowly increased so that by the time of discharge the patient is taking a high calorie diet. He is instructed to return to normal diet a few weeks but is cautioned to eat slowly and chew at a time and to masticate well. Supportive measures as indicated are given throughout the postoperative period.

In our series postoperative complications, except for Case 3, were relatively mild considering the extensiveness of the procedure. Three cases developed partial atelectasis with associated pneumonia; all responded to forced coughing, expectorants, and sulfonamide therapy. Case 2 developed a pelvic abscess of pure *Streptococcus viridans* culture, the source of which could not be ascertained. Drainage and irrigation through a small suprapubic incision were the only treatment necessary.

PHYSIOLOGIC EFFECTS OF TOTAL GASTRECTOMY

In the removal of an organ as vitally important to the physiology of the body as the stomach, certain postoperative physiologic changes must be anticipated. These changes can be conveniently grouped as digestive disturbances and alterations in the hemopoietic system.

The digestive disturbances most commonly encountered are diarrhea, steatorrhea, dysphagia, and biliary regurgitation.

Diarrhea after total gastrectomy is reported frequently. Clute reported 2 out of 3 cases with diarrhea, one of which responded somewhat to dilute hydrochloric acid. In our series only 1 patient, Case 5, developed diarrhea. This symptom began as soon as the patient started to take food orally and persisted for approximately 2 months. It ceased spontaneously and has not recurred to date. Hydrochloric acid was not beneficial. The cause of this diarrhea is difficult to explain. Golden removal of hydrochloric acid from the upper gastrointestinal tract must be a factor, since reported cases responded to its administration. Ivy showed that enteritis frequently causes diarrhea after total gastrectomy in dogs and attributed it to the lack of attenuation of the bacterial flora of the upper gastrointestinal tract. This is undoubtedly a factor, but loss of gastric enzymes must also be involved, since hydrochloric acid does not affect the diarrhea in many cases.

Persistent steatorrhea develops after total gastrectomy. Rekers and others, in a comprehensive study, showed that the fat content of the stools was greatly increased after total gastrectomy and that only pancreatic enzymes consistently restored the fat content of stools to normal. Three cases in our series showed definite evidence of

TOTAL ABDOMINAL HYSTERECTOMY AND THE "OCCASIONAL OPERATOR"

EUGENE A. GASTON M.D. F.A.C.S. Framingham, Massachusetts

TOTAL hysterectomy as the operation of choice in the treatment of benign diseases of the uterus has become increasingly popular during recent years. Hysterectomy with removal of the cervix is technically more difficult than without removal of the cervix, yet statistics from large gynecological clinics have shown the more radical operation to be little if any more dangerous (1-3 8 9 12 14-16 20 21). In these institutions the operations are performed by or under the supervision of surgeons who attain great technical skill by repetitiously performing the operation many times (in some cases several hundred times) each year.

It is proper that new surgical techniques should be developed and first evaluated in large clinics staffed by surgeons of experience. It is probable however that a large part of the total of pelvic surgery is done not in such institutions but in small community hospitals where operators are confronted with the problem of hysterectomy but a few times each year. The question arises as to whether the total operation should be advised for surgeons of such limited experience. The recorded opinions are of but one conviction. In fact, in the literature of no other operation has the 'occasional operator' (variously estimated as the surgeon who does from 6 to 24 hysterectomies per year) been so consistently and emphatically warned against attempting to emulate the pioneers (2 6 10-12 16-18 20).

Phaneuf states: "In the hands of a well trained pelvic surgeon who performs a hundred or more hysterectomies yearly, there is no great difference between the two methods in mortality and morbidity but such is not the case in the hands of an operator who performs but few of these operations, probably 6 or 12 yearly." Similarly Foss and Babcock state: "The surgeon who performs 1 or 2 hysterectomies a month should adhere to the supravaginal procedure. Such a man cannot consider himself broadly experienced. In all probability the man who performs a hundred or more each year should be able to carry out the total operation expertly with a mortality no greater

than that of the surgeon who adheres to the less formidable procedure. Even Phillips and Sears, whose series comprises only 32 cases of total hysterectomy state: "The untrained and unexperienced will, of course, have a considerably higher mortality in total hysterectomy."

To a supposedly learned profession advice to the effect that the surgeon should be conversant with pelvic anatomy and with a satisfactory technique for removal of the cervix (11 14 16) may be regarded as superfluous. Given this fundamental background the following study is presented in an effort to show that total hysterectomy may be safely utilized by the surgeon who does only an occasional hysterectomy.

GENERAL CONSIDERATIONS

In a practice limited to general surgery in a community of 25,000 population, the problem of hysterectomy has presented itself 130 times in a 7 year period ending May 31, 1944, an average of 18.6 hysterectomies per year. Of these 130 cases 20 or 15.4 per cent of the entire series, were done by the vaginal route all for proctocutanea and 110 or 84.6 per cent of the entire series, by the abdominal route. Of the 110 abdominal hysterectomies 39 were supracervical (35.5 per cent) and 71 were total (64.5 per cent). Of the total hysterectomies, 65 were performed for benign lesions and 6 for malignant growths. These 6 cases have been excluded from the present series because all are agreed that in situations which demand hysterectomy for the control of malignant growth of the corpus or of the adnexa, total hysterectomy should be done. Patients with such malignant lesions belong to an older age group and from the very nature of their disease, are, in general poorer surgical risks than the younger patients with benign pathology. It is not logical to include the malignant lesions with the benign in evaluating the risk of total hysterectomy done for benign disease, although this has been done in a great many of the reported series.

Table I shows the yearly distribution of supracervical and total hysterectomies in the 104 abdominal cases done for benign disease. The latter operation was first undertaken in January 1939. During the succeeding 18 months, 11 total ab-

From the Surgical Service of the Framingham Union Hospital, Framingham, Massachusetts.

in selected cases through considerable decrease in mortality.

3. An evaluation of the procedure is not possible at this time because of the limited number of cases presented and the short period of postoperative observation.

4. Explanation of the digestive disturbances and alterations in the hemopoietic system following total gastrectomy may alter our conception of gastrointestinal physiology.

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TABLE I.—YEARLY DISTRIBUTION OF ABDOMINAL HYSTERECTOMIES DONE FOR BENIGN DISEASE

	Number of abdominal hysterectomies	Supracervical hysterectomy		Total hysterectomy	
		No.	Per cent	No.	Per cent
Year ending May 31—1938			0.0		
1939		6	14	5	3
1940			5		17.5
1941					8.6
1942	5			5	6
1943	20		20		20
1944	18		5		
Total	124	20	15.7	5	

dominal hysterectomies were done for benign disease. The clinical impression was obtained that the postoperative reactions were not materially different from those encountered after supracervical hysterectomy. Thereafter all abdominal hysterectomies done for benign disease were of the total type, unless contraindicated by the patient's general condition or by technical difficulties engendered by obesity or the pathology present. This attitude has been aptly stated by Vogt and Hamilton as follows: "We do not contend that all pelvic pathology should be treated with total hysterectomy even when surgery is definitely indicated. Some pathology is grossly so overwhelming as to suggest discretion to the operator and the few added minutes that might be required to remove a cervix in a patient already potentially shocked by a prolonged procedure are not warranted."

On this basis, during the past 4 years, 80.6 per cent of the cases have been total hysterectomies. The apparent yearly reduction in the percentage of total hysterectomies during this time has not been due to any lessened enthusiasm

for the operation, but is rather an example of the mathematical limitations of any small series of cases. For example, of the 4 cases of supracervical hysterectomy listed for the year ending May 31 1944 one was in an extremely obese woman with a deep pelvis and many adhesions from previous surgery which made exposure difficult. The remaining 3 were done as emergency operations under less favorable circumstances, 1 for volvulus of an ovarian cystadenoma and 2 for acute exacerbations of pelvic inflammation in middle aged married women in whom in each instance a diagnosis of acute appendicitis had been incorrectly made.

Table II shows the age distribution of all cases of abdominal hysterectomy done for benign disease. As is true in all reported series, the majority of cases were done in the 4th and 5th decades. The average age of the supracervical cases was 40 years and of the total hysterectomy cases 45 years.

The indications for total hysterectomy as determined by the major pathological findings are as follows: leiomyoma, 37 cases, or 56.9 per cent; infection, 9 cases, or 13.8 per cent; endometriosis, 7 cases, or 10.8 per cent; adenomyosis, 3 cases, or 4.6 per cent; endometrial polyps and hyperplasia, 4 cases, or 6.2 per cent; ovarian cysts, 2 cases, or 3.1 per cent; pregnancy complications, 2 cases or 3.1 per cent; perforation of uterus with intraperitoneal hemorrhage, 1 or 1.5 per cent. Chronic cervicitis was purposely omitted from the diagnoses since evidence of infection in the cervix was found in nearly all cases. Leiomyoma makes up the largest number over half of this series while leiomyoma, pelvic infection and endometriosis make up 81.5 per cent.

THE OPERATIVE PROCEDURE

It is not the purpose of this communication to describe the technique of total abdominal hysterectomy. Articles by Richardson Farrar (4), Bryan and Traube-Masson (11), Foss and Babcock, and Phaneuf are well illustrated. Gest has described a combined vaginal and abdominal technique. The technique used in this series is that described by Meigs by which accurate hemostasis during removal of the cervix is easily obtained. This is the most important single consideration in the entire operation. The surgeon who works under direct vision in a dry field has little fear of injuring the important surrounding structures.

Several points in the conduct of the operation seem worthy of emphasis. The importance of adequate preparation of the vagina has been

TABLE II.—AGE DISTRIBUTION

	Supracervical hysterectomy		Total hysterectomy	
	No. cases	Per cent	No. cases	Per cent
10-20				
20-30	14			
30-40	6			13
40-50	5		5	
50-60				
Average age	40 of 37	(30 cases)	45 of 37	(1 case)

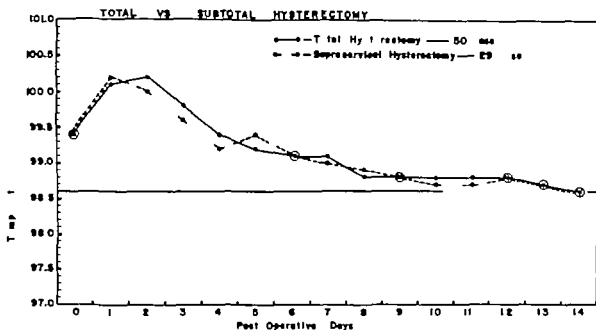


Chart 1 Average of highest daily temperature recordings in uncomplicated total and supracervical hysterectomies.

stressed by Farrar (3) who states that peritonitis will probably always remain a possible complication until the vaginal mucous membrane is as carefully prepared before operation as is the skin. This has been satisfactorily accomplished by placing the patient in the lithotomy position and thoroughly scrubbing the perineum and vagina with soap and water followed by 70 per cent alcohol and aqueous zephiran. The bladder is then emptied with a catheter introduced under strict aseptic precautions. The uterus is curetted and if infection or malignant growth is present the cervix is closed tightly with a suture. Usually the cervix is not closed. If a minor amount of perineal relaxation is present, this is immediately repaired by a simple method requiring 15 or 20 minutes. If a second or third degree laceration requires a more extensive repair this is deferred until after the abdominal hysterectomy has been completed. If the patient's condition is not ideal at the end of the abdominal operation, the perineorrhaphy may be deferred for several days. The importance of repairing even minor degrees of perineal relaxation at the time of or soon after hysterectomy has not been sufficiently emphasized. In this series of 65 total hysterectomies, 36 (55.4 per cent) had the perineum repaired. Of these, 33 were done at the time of hysterectomy and 3 were delayed until about the end of the first postoperative week.

Due to the development of estrogenic substances which are effective when taken by mouth the tendency in this series has been to be in

creasingly radical in the removal of the adnexa along with the uterus. Thus in 64.6 per cent of the total hysterectomies both tubes and both ovaries were removed while this was done in only 48.5 per cent of the supracervical hysterectomies. Most of the supracervical cases were operated upon in the earlier years of the series. No complications related to removal of the adnexa have been encountered. The same may be said for routine removal of the appendix which is always done if it can be easily delivered into the operative field. Appendectomy was performed in 47.7 per cent of the total and in 37.1 per cent of the supracervical operations in this series.

One of the objections that has been raised to total hysterectomy is the additional operating time required for removal of the cervix. In our series, the total time required to perform total hysterectomy including perineorrhaphy in 64 cases averaged 103.8 minutes for the abdominal operation only 73 minutes in 37 cases. Supracervical hysterectomy including perineorrhaphy averaged 87.7 minutes in 25 cases and the abdominal operation only 73.6 minutes in 14 cases. It should be noted that operating time in these cases means all of the time consumed from the time the anesthesia has been induced until the dressing is in place. The average of all cases with records sufficiently complete for satisfactory analysis shows total hysterectomy to require 16.1 minutes more than supracervical hysterectomy yet 50.7 per cent of the former had immediate perineorrhaphy while this was done in only 11.4 per cent

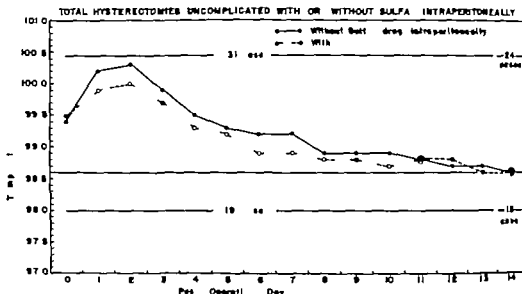


Chart 1 Average highest daily temperature recordings / uncomplicated total hysterectomies, with and without the intraperitoneal implantation of sulfa powder

of the latter. Undoubtedly the time required for perineorrhaphy accounts for a large part of this difference.

In 37 cases of total and in 14 cases of supracervical hysterectomy the anesthesia chart indicated accurately the duration of the abdominal operation from the time the incision was started until the dressing was in place. While the number of cases is small, there is remarkably little difference in the operating time.

MORBIDITY

The average postoperative temperature reaction in 50 uncomplicated cases of total hysterectomy is compared with that of 29 similar cases of supracervical hysterectomy in Chart 1. It is evident that there is little difference between the two.

Chart 2 shows a similar comparison of uncomplicated cases of total hysterectomy with and without the application of 5 grams of sulfanilamide or sulfathiazole powder to the pelvic peritoneum. The clinical impression has been gained that those receiving the drug have had a somewhat easier convalescence. This impression is confirmed by the lower temperature reaction.

Table III enumerates the postoperative complications that have been encountered in this series. As expected, cystitis was seen most frequently in both the total and supracervical groups. The fact that it was seen twice as frequently after supracervical hysterectomy is of some interest. Probably the small number of

cases in each group make this difference more apparent than real. However, during the past 3 years special attention has been directed to the postoperative care of the bladder and this may also have played a part in the improved results. This care has consisted of constant urethral catheter drainage for a period of 4 to 7 days after operation. A real effort is made to keep the end of this catheter and the attached drainage tubing sterile. The bladder is thoroughly irrigated three times daily with a saturated aqueous solution of sulfanilamide heated to body temperature. After removal of the drainage apparatus, the bladder is emptied with a catheter introduced under rigid aseptic precautions, every 6 to 8 hours, until the patient voids in amounts exceeding 6 ounces. Thereafter catheterization and bladder irrigation is done once daily until the residual urine is less than 1 ounce. Sulfanilamide in doses of 0.5 gram are given by mouth four times daily starting the day after operation and continuing until a day or two after catheterizations have been stopped.

The remaining postoperative complications require little comment. The bleeding from the vagina in 1 case, following total hysterectomy was not severe and responded promptly to the packing of the vagina with gauze. The only case of peritonitis followed supracervical hysterectomy done for chronic pelvic inflammation. Peritonitis in this case was of a low grade of virulence, was confined to the pelvis, and was followed by complete recovery.

FOLLOW UP STUDIES

Of the 65 cases of total hysterectomy 7 institutionalized patients have been excluded from the follow up study. Of the remaining 58 cases 56 have been personally examined from 2 to 66 months after operation. The average follow up period was 23.2 months.

One case of postoperative ventral hernia developed during the first year after total hysterectomy. This caused sufficient symptoms so that operative repair was required and was followed by satisfactory healing. The abdominal wounds in the remaining 55 cases have remained well healed.

In a few cases a vaginal discharge has persisted after operation. In every case this has been found to be due to exuberant granulation tissue at the upper end of the vagina. Removal of the granulation tissue in the office followed by cauterization with silver nitrate has in every case, resulted in prompt and permanent healing. The vaginal support in every case has been found to be satisfactory. There has been no prolapse of the vagina.

Particular attention has been paid to the length of the vagina at the time of the follow up examinations. While accurate measurements of the elastic vaginal tube are not practicable the clinical impression as to whether shortening has followed operation has been recorded in every case. In 4 cases (7.1 per cent) evidence of slight shortening was found. That this shortening was slight in amount and of no functional importance is indicated by the fact that 3 of these women were married and had experienced no dyspareunia as a result of the shortening. The fourth patient was unmarried. In none of the cases was persistent pelvic tenderness found although this too was carefully sought for and recorded in every instance.

An effort was made to evaluate the effect of total hysterectomy on the sex life of each of the 43 patients whose husbands were living and well. Satisfactory information as to the libido before and after operation was obtained in 25 cases. Of these 11 patients had a normal libido before operation of whom 8 found no change after operation. Six of these 8 patients had all ovarian tissue removed at the time of hysterectomy. Fourteen patients reported poor or absent libido before operation and all of these found no change after operation. Ten of these patients had all ovarian tissue removed. Thus 22 of 25 patients (88 per cent) found no change in libido. Of the 3 patients who found the libido lessened or absent after operation 2 had both ovaries removed and the third had 1 ovary removed.

TABLE III — POSTOPERATIVE COMPLICATIONS

Complication	Total hysterectomy (65 cases)		Supracervical hysterectomy (30 cases)	
	N Cases	Per cent	N Cases	Per cent
Cystitis	4	6	5	8
Deep thrombophlebitis (without emboli)	3	4.6		6
Superficial thrombophlebitis		5		
Pulmonary embolism 11th recovery		5		
Wound sepsis (superficial)	3	4.6		5
Pulmonary telecystitis		5		
Bronchopneumonia		5		
Surgical shock		5		5
Postoperative vaginal bleeding		5		
Pelvic peritonitis				6

Information concerning orgasm before and after operation was obtained in 39 cases. Twenty five patients reported satisfactory orgasm before operation of whom 20 (80 per cent) found no change after operation. Of these 20 cases 14 (70 per cent) had both ovaries removed. Of the remaining 5 patients all found orgasm absent after operation. Two attributed this to perineal pain, 1 to fatigue and 2 to absent libido. Three of these 5 patients (60 per cent) had both ovaries removed.

Of the 14 cases reporting unsatisfactory orgasm before operation all stated that the same condition existed after the operation. Thus, of the 39 cases 34 or 87 per cent found that operation caused no change in the orgasm.

Thirty five patients gave information concerning the presence or absence of dyspareunia. In none of these was dyspareunia present before operation. Five patients (14 per cent) stated that intercourse was painful after operation. All described the pain as located at the introitus. All of these patients had perineorrhaphy performed at the time of hysterectomy and this probably accounts for the discomfort experienced. None of these patients showed evidence of pelvic tenderness or of shortening of the vagina.

MORTALITY

There were no deaths following either total or supracervical hysterectomy done for benign disease. One death followed total hysterectomy done for adenocarcinoma of the fundus, in a 69 year old woman. The patient was obese and had been bleeding for 11 months before entering the hospital. Death occurred on the seventh postoperative day following a septic course associated

with abdominal distention. Permission for autopsy was refused but clinically the patient appeared to have peritonitis. She was obviously a poor operative risk and treatment with radiation would have been better judgment.

SUMMARY AND CONCLUSIONS

A personal series of 65 cases of total hysterectomy done for benign disease is presented.

1 Important points in the conduct of the operation are emphasized.

2 Details of postoperative care are considered.

3 The morbidity and mortality rates of total hysterectomy are not significantly greater than of supracervical hysterectomy.

4 Follow-up studies indicate that about 85 per cent of patients subjected to total hysterectomy experience no change in their sex life. Significant shortening of the vagina does not follow.

5 The total operation may be safely utilized by the general surgeon of average experience.

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CARCINOMA OF THE COLON

Producing Acute Intestinal Obstruction During Pregnancy

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PREGNANCY complicated by carcinoma of the colon is fortunately so rare that authors of four standard books of obstetrics, Beck, De Lee, Stander and Titus do not mention it. Further evidence of the rarity of this lesion is given by the fact that Child and Douglas who recently reviewed 120 operations performed in a group of 40,000 pregnant women at the New York Hospital did not encounter a single case. Carcinoma of the rectum is more common and usually manifests itself by dystocia while mechanical obstruction or peritonitis is commonly the first evidence of carcinoma of the colon in pregnancy.

Der Brucke in 1940 reported 2 cases of carcinoma of the colon in association with pregnancy. In his first case signs of obstruction appeared in the 9th month of pregnancy. A 100 gram living infant was delivered after a medical induction. Laparotomy on the first postpartum day revealed a tumor which was composed of the lower part of the descending colon, the upper part of the sigmoid colon, the left tube, ovary, round ligament and the left cornu of the uterus. Eight hours after the mass had been exteriorized the patient died. Examination of the tumor mass revealed an adenocarcinoma of the colon which in addition to obliterating the lumen had invaded the surrounding tissue and the left tube and the left ovary. Obstruction developed in his second patient in the 6th month of pregnancy. At laparotomy an indurated mass was felt in the sigmoid colon. Cecostomy was performed and a biopsy specimen of the omentum showed metastatic adenocarcinoma. When premature labor ensued on the first postoperative day a premature infant who weighed 3 pounds and 2 ounces and who died within 24 hours was delivered. Two months later the patient died from cachexia and a terminal bronchopneumonia. Der Brucke further records 5 cases which he states are the only reports in the literature of the past one hundred years in which carcinoma produced obstruction during pregnancy. Three of these were due to carcinoma of the ovary, one to carcinoma of the ileum

while only one was caused by carcinoma of the colon. This last case a summary of which was published in 1927 by Fairbairn is incompletely reported but in essence a carcinoma of the colon was discovered and removed shortly after the termination of a pregnancy of 7½ months duration. Fairbairn in his original article does not mention the method of removal of the carcinoma or the outcome of the patient or child.

Evans, in 1928, performed a cesarean section because of a fixed mass which could be felt both vaginally and abdominally in the left half of the pelvis. At laparotomy this was found to be an inoperable carcinoma of the lowermost part of the sigmoid colon which was surrounded by enlarged nodes and which was adherent to the posterolateral aspect of the uterus. The baby was stillborn and the mother died on the 6th postoperative day of generalized peritonitis. There was a colloid carcinoma in the lower 4 inches of the sigmoid colon with metastases to the iliac and aortic nodes.

Mengert in 1933 described a 30 year old woman who in the 9th month of her third pregnancy developed abdominal and flank pain. Because of a large mass which could be felt by rectal examination a Porro cesarean section was done. A living 2,750 gram infant was delivered. The peritoneal cavity contained fibrin and pus. After death had occurred on the 3d postoperative day, postmortem examination revealed a perforated adenocarcinoma of the sigmoid colon which was located about 10 inches above the anus.

A similar case was described in 1937 by Fournier. After a labor of 2 hours this patient, a 31 year old quintipara, delivered a 3,200 gram living infant. Mechanical obstruction developed on the 3d postpartum day. Laparotomy revealed and postmortem examination confirmed the presence of peritonitis due to the perforation of an annular scirrhous carcinoma of the sigmoid colon.

The only recorded suggestions regarding management are made by Der Brucke and Berkeley. (2) Der Brucke writes: "Recognized in the early months the pregnancy should be disregarded and the neoplasm treated as under all other conditions. Recognized after viability, the fetus should be delivered from below and laparotomy per-

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Fig. Frequent flat plat of the abdomen high above the site of obstruction. The sigmoid colon just below the left iliac crest.

formed for the correction of the obstruction immediately thereafter. Berkeley Bonney and MacLeod describe their management under four phases: (1) acute obstruction, (2) the presence of an operable tumor prior to the development of the obstruction, (3) an inoperable lesion without obstruction, and (4) dystocia. In the presence of an acute obstruction they recommend, regardless of the duration of pregnancy, hysterotomy, colostomy, and later resection. In the presence of an operable carcinoma uncomplicated by obstruction they suggest (1) colostomy and resection or (2) hysterotomy, colostomy and later resection or (3) hysterectomy and resection. If the carcinoma is inoperable but no signs of obstruction are present they prefer hysterotomy and colostomy in the early months of pregnancy, while in the later months they recommend temporizing till viability at which time a cesarean section and colostomy are performed. If dystocia is present they prefer a cesarean section and colostomy.

CALL REPORT AND DISCUSSION

C. F. White, 3 years of age, tripara, quartigravida, as due on September 2, 1941. 938 lb. She had rheumatic fever with chorea, but, at present, apart from mitral

stenosis and insufficiency she was well compensated and as classed II C (New York Heart Association classification). There was no history of diarrhea, constipation or bloody stools. Four days before admission in June, 1944, while in the 6th month of pregnancy she developed recurrent cramps in the left flank which radiated downward and across the abdomen. She had not had bowel movement for days prior to admission. N. status was passed. Enemas are given without result. Physical examination revealed: tumor high as enlarged (the umbilicus and high contained an active baby estimated at 3,500 grams). The upper abdomen was distended by dilated loops of bowel arranged in ladder patterns. Peristaltic waves were seen. The catheterized rectum contained only few fecal cells, the leukocyte count 6 thousand and flat plate of the abdomen (Fig. 1) showed loops of dilated bowel about

site of obstruction in the sigmoid colon. Acting on the diagnosis of mechanical obstruction an exploratory laparotomy was performed by one of us (J. W. L.) on June 14, 1944. A left lower rectus incision was made under open drop ether anesthesia. The tumor was found to be 6 months gravid. The transverse and descending colon were dilated to twice their normal size and were slightly edematous. About 10 centimeters beyond the junction of the descending and the sigmoid colon was found a hard, annular lesion 10 centimeters in length. The bowel below the lesion was collapsed. There was no evidence of lymph node metastasis or of peritoneal implantation. Because of the extreme distention and the obvious carcinoma, it was deemed best to perform only transverse colostomy at this time. Therefore, the left rectus incision was closed and the midportion of the transverse colon brought out through an upper right rectus incision. A rubber catheter was inserted into the colon for immediate decompression. Ten weeks later the left lower rectus incision was opened, the tumor retracted toward the midline and an aseptic end-to-end anastomosis was done over Kocher clamps, with interrupted silk sutures, after about 5 centimeters of the sigmoid colon had been removed. After the anastomosis 4 grams of sulfanilamide were sprinkled into the peritoneal cavity and an additional 4 grams were placed in the lumen of the wound which was closed (without drainage) by interrupted sutures of silk. Sulfadiazine had been administered for 24 hours prior to the resection and was continued during the first 7 postoperative days. The adenocarcinoma (Fig. 2) was an annular lesion which had produced complete obstruction. Histological examination of the accompanying lymph nodes failed to reveal any evidence of metastasis. Ten weeks later on July 3, 1944, the colostomy was closed. Recovery from each of the operations was uneventful. No signs of premature labor appeared during any of these procedures, and 7 weeks after the first operation she was discharged and followed in the clinic. Before her obstetrical course was normal, 10 months prior to term when she entered the hospital because of rectal bleeding. After distension the stools were mucoid, but were never grossly bloody. Because of the proximity to term, examinations of the colon were deferred and the patient was observed in the hospital until labor ensued. After labor of 6 hours and 40 minutes a 3,340 gram infant was delivered. The puerperium was afebrile. Proctoscopy in the early puerperium revealed no lesion. (Itkin 1935) 10 centimeters of the anus. Barium enema, however, showed an annular constricting lesion in the descending colon. Just much as there was no mucosal defect, it was thought that this represented only the site of anastomosis, but further x-ray examination will be necessary to eliminate the possibilities of recurrence or spasm. Several nodules, measured by 5 centimeters, were felt in the distants of the rectum muscles. These physical and x-ray findings, like

not conclusive are suggestive of recurrence or metastases. Hence our prognosis after delivery is less optimistic than it was at the time of resection.

This case report emphasizes several surgical principles in the management of large bowel neoplasms during pregnancy. Child and Douglas have stated recently: "Pregnant women tolerate even major surgical procedures quite as well as the nonpregnant" and that "when the surgical disease however becomes complicated by peritonitis the outlook is unfavorable and the maternal and fetal mortality high." This patient withstood the three stages which were necessary for the relief of the acute intestinal obstruction and the removal of the carcinoma of the sigmoid as well as any nonpregnant patient. Each wound healed satisfactorily and the total hospital stay was 7 weeks. The gravity of peritonitis in the pregnant woman led to the choice of the three stage method and the aseptic anastomosis. An alternate method would have been to perform a Mikulicz type of exteriorization of the loop of sigmoid with immediate resection and opening of the proximal loop for the alleviation of the complete obstruction. The method chosen was the closure of the left lower rectus wound as soon as the diagnosis was established and the immediate performance of a transverse colostomy. No contamination of the peritoneal cavity occurred because only gas was present in the transverse colon whereas the sigmoid and descending colon contained formed feces.

Another point of importance in the management by the three stage procedure is the type of anastomosis of the sigmoid colon following the resection of the carcinoma. Many surgeons prefer the open side-to-side or open end-to-end techniques but we have in practically all cases employed the aseptic end-to-end anastomosis over Kocher clamps with silk as the suture material. Wangenstein has stressed the value of such aseptic end-to-end anastomosis in operations on the colon. Because of the great danger of peritonitis in the pregnant woman we believe that the aseptic technique contributed to this patient's uncomplicated convalescence. The great distention of the bowel above the carcinoma would have further contributed to the possibility of infection of the peritoneum had an open anastomosis been done. A Mikulicz procedure would have been technically difficult because of the relatively short mesosigmoid and because of the large size of the uterus. Further a secondary closure of the Mikulicz operation is not infrequently necessary thus nullifying one of its assets—the one stage



Fig. 2. Annular adenocarcinoma of the sigmoid colon.

operation. Though both Der Brucke and Berkeley state that the uterus should be evacuated either by vaginal delivery, hysterotomy or hysterectomy, we found that the pregnant uterus did not interfere significantly with the technical performance of the operation. Experimental (11) and clinical (10) evidence indicate that the sulfonamide derivatives are of value in the prevention of peritonitis and of wound infection. Sulfanilamide was used at the time of the resection both intraperitoneally and in the wound. Sulfadiazine had been given for 24 hours before operation and was continued for the first week after the resection.

Some authors have attributed the lack of early symptoms when carcinoma of the colon coexists with pregnancy either to the fact that the pregnancy masks the symptoms or they are mistakenly ascribed to the pregnancy. Our patient however had no symptoms until the acute obstruction developed. Christopher states that acute obstruction is the first manifestation in about 5 per cent of the patients who have carcinoma of the left side of the colon. From analyzing the few recorded cases, carcinoma of the colon may manifest itself in pregnancy by bowel symptoms which is rare by obstruction as in our patient by peritonitis, or by dystocia. The latter is most common if the carcinoma is low in the sigmoid colon where it joins the rectum. When the

first manifestation is peritonitis or dystocia the outcomes so far recorded have been fatal. To our knowledge this is the first instance of carcinoma of the colon producing acute intestinal obstruction in pregnancy in which both mother and baby have survived.

SUMMARY

Because of its rarity and because of some unusual features in its surgical management a case of carcinoma of the colon which produced acute intestinal obstruction during pregnancy has been discussed. For comparison all the reported cases of carcinoma of the colon complicating pregnancy have been briefly reviewed. To our knowledge our patient is the only one who has survived. We attribute this to the following facts:

- 1 The carcinoma first manifested itself by the presence of obstruction rather than by peritonitis or dystocia.
- 2 The carcinoma was in an operable state.
- 3 Multiple stage procedure was carried out i.e. preliminary transverse colostomy followed by resection of the lesion and subsequent closure of the colostomy.
- 4 Aseptic anastomosis was performed.

- 5 Use of sulfonamide derivatives prior to, during and after the resection was liberal.

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DEFECT OF THE ANTERIOR MEDIASTINUM

Successful Surgical Repair

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OPENINGS in the anterior mediastinum with direct communication between the two pleural cavities, are very rare congenital abnormalities. Kupfer studied mediastinal lesions in 6,000 autopsies and did not observe such an anomaly. In 1939 Ochner, DeBakey and Murray reported a case of congenital absence of the anterior mediastinum (associated with a left diaphragmatic hernia). They could find but 9 other reports of human subjects who were suspected of having a passageway connecting the two pleural spaces. We have reviewed the literature since that time and have uncovered no additional examples of the condition. In view of the rarity of the defect it appears worthwhile to assemble pertinent facts which have been previously set forth by other authors and also to put on record a case which is apparently the first in which an anterior mediastinal opening has been surgically repaired.

SURVEY OF LITERATURE

In most of the previously described cases, absence of the anterior mediastinum caused little or no symptoms and was discovered only because there was evidence of a communication between the two pleural cavities. In 1903 Fraentzel observed at autopsy an individual with tuberculosis of the left lung who had sustained a spontaneous pneumothorax. A mediastinal opening had allowed air to escape into both pleural cavities, producing a bilateral pneumothorax and collapse of both lungs. In 1919 McCallum reported a case with tuberculosis of the right lung. During the production of an artificial pneumothorax, air was seen (by fluoroscopy) to pass also to the contralateral side. In 1924 Walsh and later Loganston and Rozorov described 2 similar cases. In 1925 Dumarest and Bonafe reported the findings in a 35 year old man with tuberculosis of the left lung. After artificial pneumothorax treatment had been started on the left side the patient complained of dyspnea and pain on the right side of the chest. Bilateral pneumothorax was evident by roentgenograms and was further attested to by aspiration of air from both pleural cavities. In 1930 Jullien

studied a 24 year old woman with pulmonary tuberculosis. During injection of air into the right pleural cavity the left lung became collapsed but the right did not. Apparently the right lung was held to the chest wall by adhesions but air could pass over into the left side of the thorax. Ameuille noted a similar situation in which lipiodol was introduced into the right pleural cavity and was then seen to pass anterior to the heart and to run over into the left pleural space. In 1933 Smith and Willis reported the findings in a tuberculous patient. Needles were introduced into both pleural cavities and a rise in intrapleural pressure was noted during injection of air on opposite side.

In each of the instances cited the presence of a pulmonary tuberculosis raises the possibility that an interpleural communication could have resulted from tuberculosis and necrosis of mediastinal tissue. In 1926 Le Waki made initial observations on a person with apparent interpleural communication in the absence of demonstrable tuberculosis. This individual suffered a spontaneous right pneumothorax while vigorously using an adding machine. One week later collapse of the left lung occurred with evidence by roentgenogram of increased collapse of the right lung. It is not entirely clear whether this man actually possessed a mediastinal opening which allowed air to pass between the two pleural cavities or whether he sustained bilateral spontaneous pneumothoraces with an intact mediastinum. Ochner, DeBakey and Murray fully and clearly described anatomical findings which without question represented a congenital abnormality of the mediastinum. This 18 month old child was operated upon for a left diaphragmatic hernia. During the course of operation—by a transthoracic approach—an extensive and free communication was observed between the two pleural cavities. The entire anterior mediastinum was absent and a wide view of the right hemithorax could be obtained from the left sided chest wound. The pericardium and great vessels lacked their normal attachment to the posterior aspect of the sternum. The opening between the two pleural cavities was so large that in effect they constituted a single chamber. An identical malformation of the mediastinum existed in the patient herewith presented.

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Fig. 2. Preoperative roentgenogram of chest showing emphysematous right upper lobe. This lobe bulges over into the left side of the thorax (outlined by arrow.)

EMBRYOLOGIC AND ANATOMIC CONSIDERATIONS

The primary endodermal portions of the respiratory tree are developed in a median mass of mes-



Fig. 3. Preoperative, lateral film of chest, showing anterior mediastinal defect. Wide, air filled space between anterior border of pericardium and back of sternum.



Fig. 4. Preoperative, left anterior oblique roentgenogram following lipiodol injection. The right upper lobe is cystic pharynx. The middle and lower lobes are compressed.

enchyme, dorsal and cranial to the main pericardial cavity. The original right and left stem beds of the lungs grow out laterally into their respective pleural cavities, carrying before them dome-shaped investments of mesoderm. As the lungs enlarge, they find room by burrowing into the spongy tissue of the adjacent body wall. This advance splits off an increasingly extensive pericardium from the thoracic wall and allows the lungs more and more to flank the heart on each side. When the pleural cavities are completed the mesothelial coverings of the lungs become the visceral pleurae. The corresponding layers lining the thoracic wall constitute the parietal pleura. Before birth the lungs are relatively small and compact. They occupy only the dorsal portions of the thorax, while the anterior mediastinum is quite extensive and is very broad. With the onset of breathing at birth, the lungs distend with air and assume a more anterior position—this readjustment taking place by compression and narrowing of the anterior mediastinum.

The mediastinum lies between the right and left pleurae, in and near the median sagittal plane of the chest. It extends from the sternum in front to the vertebral column behind, and contains all the thoracic viscera except the lungs. It may be divided for purposes of description into two parts: the *superior mediastinum* which lies above the upper level of the pericardium, and the *inferior portion* which includes the structures and spaces be-

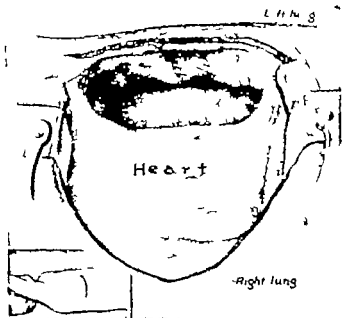


Fig. 4. Drawing of operative field. There is a broad opening between the sternum and the pericardium. When the chest was opened, the ballooned-out, right upper lobe was found prolapsed over through this opening. When this lobe was withdrawn, the operator could look directly over at the left lung, as shown in this drawing.

low the upper border of the pericardium. This lower portion is again subdivided into 3 parts, viz: that in front of the pericardium, the *anterior mediastinum*; that containing the pericardium and its contents, the *middle mediastinum*; and that behind the pericardium, the *posterior mediastinum*. The anterior mediastinum is bounded in front by

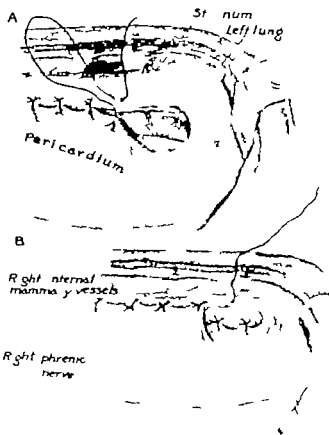


Fig. 5. Surgical repair of mediastinal defect. A, Pericardium and great vessels anchored to back of sternum with interrupted silk sutures. B, Second row of sutures being placed.



Fig. 6. Postoperative roentgenogram of chest (Compare with Fig. 3).

Fig. 7. Postoperative lateral roentgenogram of chest. The retrosternal space is now obliterated. (Compare with Fig. 3.)



Fig. 7



Fig. 8. Photograph of patient, year after operation, showing excellent general physical status.

the sternum laterally by the pleurae, and behind by the pericardium. It is narrow above, but widens out a little below. It contains a quantity of loose areolar tissue, some lymphatic vessels, scattered lymphatic glands, and the small mediastinal branches of the internal mammary arteries. The substance of the anterior mediastinum is such that it offers relatively little resistance to displacement and hence it may bulge to either side. Her herniation through the mediastinum is a well recognized phenomenon and has frequently been seen in conjunction with lesions which disturb the normal pressure relationships on the two sides of the chest. Under such circumstances a lung which bulges into the contralateral side of the thorax is always covered by its parietal pleura.

Distinct from subjects with a mediastinal hernia are those rare individuals in whom an actual communication exists between the two pleural spaces. This latter congenital type of anatomical curiosity is probably best explained on the basis of an over-encroachment of the lungs in a forward and then medial direction during fetal life, so that the yielding anterior mediastinum becomes compressed and resorbed. If such encroach-

ment is of only moderate severity a septum-like type of anterior mediastinum could presumably result—such as that normally present in the dog. If, however, the encroachment is more advanced, the pleurae which appose one another may disappear and an opening of variable size can develop between the two cavities.

A large communication between the pleural cavities, *per se*, probably causes no physiological abnormalities or clinical symptoms. Foundation for this statement can be found in the postoperative course of the patient described by Ochsner, De Bakey and Murray who had a repair of a left diaphragmatic hernia but no closure of the mediastinal opening. The child had no subsequent symptoms and roentgenograms showed no mediastinal or pulmonary shift. In contrast, a mediastinal opening is a definite hazard if in addition there is some associated malformation or disease which disturbs the pressure equality which normally exists in the two sides of the chest. An example of such a mechanism is demonstrated by our patient who in conjunction with the mediastinal opening, had a defective right upper lobe bronchus which allowed air to enter and then become entrapped in this lobe. This ballooned and the emphysematous lobe prolapsed through the anterior mediastinum and induced violent spells of respiratory distress.

CASE SUMMARY

In June, 1930, L. H. 7, 7 week old, white, female infant entered the Children's Hospital with chief complaint of "difficulty in breathing" since birth. Delivery had been normal, but the baby was almost constantly cyanotic during the first few weeks of life. After that period, there were frequent episodes of rapid breathing, somewhat labored respiration, and concurrent cyanosis of moderate degree. These attacks varied in length from a few minutes to several hours. The intervals between these, the child appeared to be normal in every way.

Physical examination revealed obvious respiratory distress. Breathing was rapid and staccato in character, with definite intercostal retraction during the inspiratory phase. Crying would produce a moderate degree of cyanosis. On the left side of the chest, there was dullness to percussion and diminished breath sounds over the apex anteriorly and posteriorly; at the base, the sounds were harsh but otherwise normal in character. Throughout the right chest, particularly over the upper half, the percussion note was distinctly tympanic; over the superior one half of the lung the breath sounds were diminished and distant, while at the base they were of normal intensity and quality. The heart was markedly displaced to the left.

The white blood count was 3,000 cells per cubic millimeter. Red blood count was 4,600,000 cells per cubic millimeter. Hemoglobin was 95 per cent. Blood smear and differential count were normal. The urine was normal. Microfilaria test was negative. Tuberculin test (1:100) was negative.

Roentgenograms and fluoroscopic studies revealed an oblong, air-filled structure in the anterior and upper portion of the right pleural cavity which extended over behind the sternum, all to the left of the midline. Within the

periphery of this highly translucent area, a few indistinct, fine trabeculae could be seen—indicating that the structure was not a simple, air filled sac but that it contained some emphysematous pulmonary tissue. The lower one third of the right pleural cavity and the outer two-thirds of the left pleural cavity contained lung tissue of normal aeration and density. The heart was displaced to the left. The roentgenographic picture suggested that we were dealing with a congenital cyst of the right lung, which communicated with a bronchus. Furthermore, the bronchus was thought to have a ball valve obstruction, because air appeared to enter the cyst and become entrapped therein. The ballooning of the "cyst" toward the left was assumed to represent a true, anterior mediastinal hernia—that is, it was thought to be covered by parietal pleura as it bulged over through the mediastinum and to the left of the sternum.

On the fourth hospital day there was an especially severe episode of respiratory embarrassment which prompted aspiration of the "cyst" under fluoroscopic control. A needle was inserted through the right second intercostal space anteriorly and 90 cubic centimeters of air under considerable pressure were removed. This procedure, instead of improving the child's condition, caused cyanosis to become much more severe and indeed alarming. Fluoroscopy now showed that there was a bilateral pneumothorax. Apparently the needle puncture of the "cyst" wall had permitted air to escape into the right pleural cavity, and a portion of this air had passed over into the left pleural space. We now had indubitable evidence for the first time that a free communication existed between the two pleural cavities. In order to tide the baby over the current emergency an intercostal catheter was quickly inserted into the right side of the chest and all free air sucked out of the pleural spaces.

On the 6th hospital day the thorax was explored by Dr. Thomas H. Luman. Exposure was obtained through a right anterolateral approach in the fourth interspace. When the chest was entered, no cyst or accessory lobe was observed. Instead the right upper lobe of the lung was emphysematous to an extraordinary degree and represented the radiolucent structure which had previously been discovered by fluoroscopy and by x-ray film studies. This greatly distended right upper lobe ballooned over behind the sternum and protruded into the left side of the chest. When it was manually withdrawn from this location an extensive defect or "absence" of the entire anterior mediastinum, from the diaphragm up to the sternal notch was found. The pericardium and great vessels formed the posterior wall of this wide aperture between the two pleural spaces. The left lung could be viewed directly. Because of the exposure of both lungs to atmospheric pressure, the entire left lung and the right middle and lower lobes became quite collapsed. (The distended right upper lobe did not collapse a fact which gave further evidence of some abnormality or valve like mechanism in the right upper bronchus.) The baby's condition became so critical that it could be only partially controlled by the positive pressure, which was being administered through the anesthesia face mask. Because of the prostration of the child nothing more was done, and the chest was quickly closed. The postoperative condition was precarious, but with sedation and use of an oxygen tent, the baby gradually improved. She was discharged on the 30th postoperative day.

The subsequent course of this child for the next 4 years was one of transient episodes of respiratory distress. These sometimes appeared two or three times a day, usually they occurred several times a week, but at some periods she was symptom-free for a month or more. Individual attacks lasted from a few minutes to more than an hour. During these spells the respirations were very rapid and sometimes grunting and labored. The color became poor and mild to

moderate cyanosis was often observed. The child would sometimes sweat profusely and then after the attack would sink off into a deep sleep in an exhausted state. Unquestionably there seemed to be an intermittent obstruction of the right upper lobe bronchus which temporarily permitted air to enter this lobe and distend it under considerable pressure. The enormous right upper lobe could then compress the remaining portion of the right lung and could also impinge upon the left lung to a lesser degree. A part of the picture may have been produced by direct pressure on the heart and great vessels. The child got no relief until in some way the valve-like action in the right upper bronchus was spontaneously released and the overdistended lobe was thereby deflated.

Frequent roentgenograms (Figs. 1, 2 and 3) showed a continuation of the picture previously described consisting, in short, of: (1) A large emphysematous right upper lobe which extended over into the left pleural cavity; (2) atelectatic right middle and lower lobes; (3) some compression of the left lung; and (4) a shift of the heart to the left. In October 1941 bronchoscopy and lipiodol study of the trachea and bronchial tree showed marked deviation of the trachea to the left and a very narrow right upper lobe bronchus. This latter did not appear to be compressed by external pressure. Instead it seemed to be intrinsically stenosed or else it was collapsed because of a congenital defect in its cartilaginous rings. The latter was thought to be the case because on this basis the intermittent symptoms could be explained on entrapment of air whenever the unsupported bronchial walls flopped together and produced a valve like obstruction. It seemed plain, too, that the child was suffering from a combination of two congenital malformations, namely: (1) an abnormal bronchus which permitted great overdistention of the right upper lobe, and (2) a wide defect of the anterior mediastinum which allowed the pressure effects to be transmitted not only onto the right middle and lower lobes, but also to the heart, the great vessels, and the left lung. Therefore, it was decided to reattempt correction of the existing congenital abnormalities, special precautions being taken with the positive pressure anesthesia to prevent bilateral pulmonary collapse when the chest was opened to atmospheric pressure.

Operation was undertaken on April 10, 1943 (by R.E.G.). The patient was now 4 years old. An intralaryngeal tube was passed down into the trachea to provide an adequate airway. A tightly fitting face mask provided a closed system through which cyclopropane was administered. The chest was opened anterolaterally in the 5th interspace on the right, the 5th and 4th costal cartilages were cut. After blunt and sharp dissection of existing adhesions, an excellent view of the interior of the thorax was obtained. The right upper lobe was quite emphysematous and protruded over through the anterior mediastinum into the left pleural cavity. When this was withdrawn, the left lung could be viewed extensively because of the great defect in the anterior mediastinum (Fig. 4). This hole was about 5 centimeters in length and ran the full length of the thorax. In anteroposterior dimensions it measured about 5 centimeters in its widest, central portion. There was no difficulty in keeping both lungs sufficiently inflated with the closed anesthesia system, employing positive pressure. The mediastinal defect was closed by drawing the pericardium and great vessels forward and suturing them with a row of about twenty interrupted fine silk sutures to the posterior surface of the sternum. The sutures grasped the sternal peritoneum and then the pericardium or the areolar tissue in front of the pulmonary artery and aortic arch (Fig. 5). This vertical line of sutures was placed just medial to the left internal mammary vessels. A second row of stitches, similar and parallel to the first, was now placed about 2

centimeters to the right of the first, just medial to the left internal mammary vessels. This procedure resulted in very satisfactory construction of the mediastinal septum.

A right upper lobectomy was now performed. The hilar structures were individually dissected and divided. The upper lobe bronchus was quite small and was not more than 4.5 millimeters in diameter. When freed adequately from overlying tissue so that it could be palpated, it was found to be soft and apparently devoid of cartilage in the section which was exposed. It could be seen to expand and collapse during the patient's respiratory efforts. Because of its soft and noncartilaginous structure, it was very easy to divide it and close it quickly with a single ligature. After the upper lobe had thus been removed, the middle lobe was allowed to turn upward so that surface of it could be touched over and buttressed against the stump of the upper lobe. When the thorax was closed, an oblique catheter was brought out through the chest wall for subsequent withdrawal of air and fluid. Gentle suction was applied to this catheter for 5 days, and it was then withdrawn. The postoperative course was entirely satisfactory. The temperature and pulse subsided to normal by the 6th day. The wound healed *per primam*. There was no emphysema or bronchial fistula. The child was discharged on the 7th postoperative day.

During the year which has elapsed since operation the patient has been entirely well and asymptomatic. A check up roentgenogram on March 7, 1944, showed the heart in normal position, the left lung fully expanded, and the right pleural cavity filled by the remaining right lower and middle lobes (Figs. 6 and 7).

In retrospect, one wonders if this patient might not have been cured by right upper lobectomy alone. While this possibility is freely admitted, it seemed to us at the time of operation that limitation of the surgical correction to lobectomy alone might be followed by subsequent distention of the left lung so that it could project over through the free space in front of the heart. In order to prevent any such future shift, it was felt that obliteration of the anterior mediastinal space was necessary to insure against any recurrence of respiratory difficulties.

SUMMARY

A brief review is given of previously reported cases of mediastinal defect and interpleural communication. Some embryological considerations are summarized as a basis for understanding a defect or 'absence' of the anterior mediastinum.

An additional case report is made of a 4 year old child who had a large opening in the anterior mediastinum, a free interpleural communication and

an anomaly of the right upper lobe bronchus. Deficiency of the bronchial cartilage allowed this airway to collapse in such a manner that air entered the upper lobe and became entrapped therein. Marked emphysema of the right upper lobe allowed it to protrude through the mediastinal opening and to invade the left pleural cavity. This child had intermittent attacks of severe respiratory distress, dyspnea, and cyanosis. These were completely relieved by simultaneous closure of the anterior mediastinal defect and removal of the anomalous right upper lobe. This is apparently the first recorded instance of surgical repair of an anterior mediastinal defect.

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EDITORIALS

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MAY 1945

ISABELLE HOLLISTER MARTIN

1863-1945

ISABELLE HOLLISTER MARTIN the widow of Dr. Franklin H. Martin passed away on March twenty third. Mrs. Martin was born in Chicago at the corner of State and Washington streets on June 21 1863 the daughter of Dr. John Hollister who was one of the founders of the Chicago Medical College which later became the Medical School of Northwestern University.

Throughout her life Mrs. Martin was actively interested and engaged in the many activities of her husband and much of the credit for the success of this Journal was due to her encouragement and stimulation of the small group of young surgeons who met with Dr. Martin and to whom he outlined the aims and ideals of his new venture. Her home was a meeting place for these men and consequently she witnessed the birth of the idea of the Clinical Congress of Surgeons and later

the American College of Surgeons and the Gorgas Memorial Institute. As a mother often feels her greatest love was for her first born and as President of the Surgical Publishing Company following Dr. Martin's death she took an active part in the publication of the Journal until the time of her death.

Unassuming and modest she had an alert inquisitive mind and a habit of dissecting quickly to the heart of a proposal and stripping it of all the finery with which it had been painted with almost irresistible enthusiasm. She acted as a balance wheel of immeasurable value to Franklin Martin and his invaluable contributions to his profession bear her unmistakable imprint.

STRICTURES OF THE COMMON AND HEPATIC BILE DUCTS

STRICTURES of the bile ducts are for the most part the result of surgical injuries to the common and hepatic ducts at the time cholecystectomy or operation upon the common bile duct is done. They are by no means uncommon. Dr. Cattell of this Clinic, will shortly report on 124 reconstructions of the bile duct on patients sent to us for repair.

These strictures could more often be avoided by the application of a few reliably simple measures—better relaxation which can be provided by properly given and supervised spinal anesthesia, longer incisions which permit easier and wider exposure, rotation of the hepatic flexure, duodenum and pylorus to the left with gauze pads and retractors as we have described, good light focused on the deep hole

in which these structures lie the individual demonstration and ligation of the cystic artery before the gall bladder is removed and finally by the clear demonstration of the relationship between the cystic, common and hepatic ducts before the cystic duct is clamped and cut. If these steps are carried out there will be far fewer of these unfortunate calamities than there are now.

After having fought my way through a large number of these operations for reconstruction of an injured common or hepatic duct in patients who have had one two three, and recently five unsuccessful previous attempts to repair the ducts I would like to suggest that the highest percentage of good results in these cases can be obtained at the time of the first reconstructive operation. In practically all of the patients we have been able to find the lower end of the duct as it enters the duodenum and follow it upward to the stricture but in many of the cases sent to us for repair the previous attempts at reconstruction have

so used up and destroyed the hepatic duct that the only remaining portion is intrahepatic and so quite difficult or impossible to use satisfactorily in its restoration.

Our best and lasting results have been obtained in the cases sent to us soon after the original injury. Our poorest results have been in those cases in which repeated unsuccessful attempts have been made to reconstruct the injured duct.

There are a number of surgeons now in all parts of the country who have had experience with the reconstruction of injured bile ducts and so I can I am sure, without suspicion of self interest, urge that such reconstructive operations upon bile ducts not be undertaken without assessing one's ability to meet the technical difficulties occurring with them and without realizing that failure of the first reconstructive operation can make the second operation much more difficult and at times one in which it is impossible to obtain a satisfactory result.

FRANK H. LANEY

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IT is generally agreed that medical history is a sorely neglected subject in the undergraduate curriculum. Students become doctors of medicine oblivious for the most part, of the great traditions of their profession. The little tome *Notable Names in Medicine and Surgery*¹ by Hamilton Bailey and W. J. Bishop affords an excellent opportunity for the popularization of medical history. While there is a tacit agreement among teachers that proper names associated with signs, symptoms, a procedure or an anatomical structure be ignored, the use of such names has persisted. Taking advantage of this the authors have penned brief biographic and historical sketches of the personalities whose names are commonly known to students and practitioners because of the associations mentioned. With each sketch is a picture of the individual concerned and one or more appropriate figures. For example the first section is fittingly concerned with Hippocrates and mention is made of the Hippocratic oath and Hippocratic facies. Galen is next considered because of The Veins of Galen, then Gabriel Fallopius because of the fallopian tubes etc. In the section devoted to Charles McBurney there are illustrations of the point, the incision and the Roosevelt Hospital where he worked. Obviously such a work to retain the advantages of brevity can not deal with all proper names that have been included in medical nomenclature. There are 81 sketches. The American reader will note the omission of Billroth (gastric resection), Mikulicz (operation) and Cushing (syndrome) when Carrel Dakin (solution) and Böhler (splint) are included.

The authors deserve great praise for making available to the profession such a delightful useful and informative little book. The manner of presentation is original and greatly enhances its attractiveness for students. This volume should be made available to all medical students and should prove an important influence in awakening general interest in medical history.

ALEXANDER BRUNSWICHO.

RADIOLOGISTS and others already familiar with the work of Brailsford welcome the third edition of *The Radiology of Bones and Joints*². The ten years interval elapsing since the publication of the first edition has seen attention focused on the recognition of early signs of various bone lesions and

has permitted the author to correlate the onset and ultimate fate of the affected bones and joints in a manner which contributes much to the instructive value of the work.

Although the book is devoted almost exclusively to the study of bones and joints due consideration is given the significance of certain other pathological changes in the soft tissues. The index is especially well prepared and deserves commendation. War necessities have made necessary the publication of many of the illustrations as line drawings. These appear in the text on relatively inferior paper but the choice illustrations are reproduced very satisfactorily on proper coated paper. References to the literature have been brought up very well to date including a satisfactory proportion of bibliographic references from the American literature. The text is exceptionally comprehensive including a consideration of every bone condition and disease whether congenital, traumatic, or pathological.

A particularly valuable phase of the author's text is revealed in his consistent effort to correlate the significance of the radiologic findings with the known facts of pathology.

JAMES T. CASE.

THE excellent book *Plaster of Paris Technique*³ by Edward Geckeler covers the subject in a very thorough manner beginning with the forms of plaster and explaining the general technique which is so essential to good cast application and continuing with the various forms and types of employment. Each of the steps following the construction of the plaster bandage to and including the application are pictorially elucidated. The errors and difficulties encountered are discussed and correction or improvements recommended. The various kinds of casts for different types of fractures and disabilities are not only discussed but are well illustrated. In my opinion this book is a contribution that is sorely needed namely teaching the undergraduates and graduates the correct technique of applying plaster. There is little that can be added with the exception of the following constructive criticism:

1. In making molds or shells for the immobilization of fractures the author states that one or two rolls are used. I do not believe that one or two rolls of plaster in a molded splint will efficiently immobilize the leg as the cast will be too thin in most instances.

2. In one of the illustrations on the immobilization of a forearm fracture the subject has a ring

¹NOTABLE NAMES IN MEDICINE AND SURGERY. By Hamilton Bailey M.D. F.R.C.S. and W. J. Bishop, F.R.C.S. London: H. K. Lewis & Co. Ltd. 1944.

²THE RADIOLOGY OF BONES AND JOINTS. By James F. Brailsford, M.D. F.R.C.P. F.R.C.S. 3d ed. Baltimore: The Williams & Wilkins Co. 1944.

³PLASTER OF PARIS TECHNIQUE. By Edward Geckeler, M.D. Baltimore: The Williams & Wilkins Co. 1944.

on the fifth finger. Because of the danger of subsequent swelling it is unwise to permit the patient to wear a ring on the injured arm or hand.

I highly recommend this book and believe that it will be beneficial to the medical profession.

JAMES J. CALLAHAN

THE reader will find *The Urinary Tract* by Kerr and Gilles a handbook of the more common and some of the uncommon lesions of the urinary tract prepared for ready reference to the student, the practitioner and the radiologist. Although emphasis is placed on the importance of correlating all the clinical and laboratory data with the roentgen findings before arriving at a final diagnosis, carrying out of this plan would lead to a too lengthy discussion of clinical and laboratory data and defeat the purpose of a book of this size. The text is divided into sections on the kidney, ureter, bladder and urethra. Most of the printed material consists of descriptions and discussions of the illustrations on the pages following the text. The work is well arranged and the illustrations well chosen and reproduced. The scope of the work is remarkably complete considering its small size.

JAMES T. CASE

IN spite of war conditions in England, the author of *Orthopaedic Surgery* has been able to revise his book. The manuscript has been carefully gone over and new ideas have been incorporated both from personal experience and from the recent literature. Many operations that the author considers are no longer useful have been deleted. Among the sections which have been revised are those on circulatory disturbances, affections of the back, knee, shoulder and foot, and infections of the hand. In all of these an attempt has been made to bring them up to date.

The author has incorporated some of Britain's in genious operations on joints and Iselin's work on infection of the hand.

This volume is a compilation of a series of lectures and clinics on orthopaedic subjects which the author has given under the direction of Professor Fraser. He has drawn freely from recognized sources. He presents the material from the point of view of the general surgeon.

The Edinburgh Medical School maintains the tradition that a surgical specialty is a branch of general surgery and that to become a good specialist one must first be a good general surgeon.

An attempt has been made to present a comprehensive survey of each subject, including the latest work. The author has purposefully avoided the details of conflicting theories.

Some of the subjects covered are congenital deformities, lesions and diseases of bones and joint, epiphyseal disturbances, affections of nerves, curative lesions of the extremities, complications of

trauma, manipulative surgery, arthrodesis and arthroplasty. Various regions of the body are discussed especially spine, shoulder, knee, and foot.

No attempt has been made to give a comprehensive bibliography but he does refer to authoritative articles on various subjects.

PHILIP LEVINE

THE author of *Principles and Practices of Inhalational Therapy* has compressed his long experience with gases for inhalational therapy into a small and very useful book. It should be available in hospital libraries for better understanding by the nursing and medical staffs of the physiological principles which are involved in gaseous therapy and of the methods which may be used.

The first paragraph on page 1 should be emphasized repeatedly in teaching medical and nursing students. Many instances of hypoxia and resulting irreparable cerebral injury could be avoided by providing an adequate airway to avoid partial respiratory obstruction and by use of additional oxygen, alone or in combination with helium or carbon dioxide.

A few minor changes in the text may be suggested. Figures 11, 1 and 4 (photographs of patients before, during and after treatment) might be amplified by line drawings for clarity. More emphasis could be placed on the wide individual variations in oxygen consumption as in hyperthyroidism where increased demand is a means of diagnosis. Toxic effects of carbon dioxide in a patient who is already damaged chemically and physiologically should be emphasized.

It is an excellent book. The bibliography includes many references to the author's articles. The descriptions and illustrations of equipment for gaseous therapy and for resuscitation are very good.

JAMES H. BERRETT

A COMPILATION of the investigated works and studies of the peritoneum over an 18 year period is presented in *Infections of the Peritoneum* by Bernhard Steinberg. As such, it is a correlation of the mass of experimental work that has been done on peritonitis by the author and the clinical management of the disease.

In the first three chapters, consideration is given to the mechanism of peritoneal infection, applied physiology of peritonitis, and the chemical changes in peritonitis. There follow chapters on pathology, progressive stages of infection, the peripheral blood, roentgen-ray diagnosis and treatment, acute peritonitis in children. The final chapters contain essentially clinical material, being devoted to special types of peritonitis as illustrated by case histories. The prevention and treatment of the disease are discussed in detail.

PRINCIPLES AND PRACTICES OF INHALATIONAL THERAPY. By Allen L. Berrett, M.D. Philadelphia, London, Montreal. J. B. Lippincott Co. 64s.

INFECTIONS OF THE PERITONEUM. By Bernhard Steinberg, M.D. With a foreword by Frederick A. Collier, M.D., M.D. New York and London. Paul B. Hoeber, Inc. 544.

THE URINARY TRACT. A HANDBOOK OF ROENTGEN DIAGNOSIS. By H. Delaney Kerr, M.D. and Carl L. Gilles, M.D. Chicago: The Year Book Publishers, Inc. 1944.

ORTHOPAEDIC SURGERY. By Walter Mercer, M.B. Ch.B., F.R.C.S. F.R.S. Baltimore: The Williams & Wilkins Co. 64s.

The author gives a thorough exposition of the progress and method of development of acute peritonitis. He devotes special attention to such topics as exudation absorption, distention, drainage, residual abscess, water balance chemotherapy and the use and effect of various drugs including a discussion of the sulfonamides.

The bibliography of peritonitis is a tremendous one, as any investigator who has worked with this subject can testify. In general practice the disease often goes unrecognized in its early stages and is commonly improperly treated in all its stages. There is probably no disease about which we know so much for which we do so little in its later stage. For these reasons, and until a sharp reduction in mortality has been obtained a volume such as this is an important contribution. The book is compact, well written, and contains an excellent bibliography.

J. R. BUCHHEIMER

IN the 5 years since the 6th edition of Flagg's *The Art of Anesthesia*¹ the war has speeded the progress of anesthesia, and the 7th edition is partially a report on this progress.

Dr Flagg's observations have prompted him to reaffirm his strong faith in ether as the backbone of anesthesia and he calls for intensive and basic training in its skillful use for both military and civilian medical men. He reports the frequency with which military men have turned to it in times of stress and hurry finding it ready and reliable when other anesthetics were not. He says that its commonly accepted postoperative ill effects are due to maladministration and its use will result in a lower morbidity, a better surgical field and less embarrassment for the anesthetist.

Dr Flagg criticizes the Army for its policy of allowing its newly trained anesthetists to exercise their judgment in each case instead of teaching them a basic routine. He points out that the training period for these men is short and that it is naive to think that they will be capable of intelligent judgment on the basis of their limited training and inexperience. In fairness to the anesthetist and his patient, the author suggests that training in the routine use of gas-oxygen-ether be given. He also considers harmful the Army order that the decision of the surgeon shall take precedence over the judgment of the anesthetist in the choice of anesthetic. It seems reasonable to believe that a surgeon's rank may not always qualify him to decide and no anesthetist should be required to handle an anesthetic unfamiliar to him in an already trying and crucial situation.

The author believes that anesthesia is threatening to become a laboratory specialty limited in activity to the hospital. When the financially attractive hospital positions are filled, he fears for the teaching and practice of anesthesia, gas therapy, and life-saving methods outside the hospitals and

urges the training of the pneumatologist in general practice.

Beside the already well known and excellent chapters there are new ones on the theory and technique of anesthesia with sodium pentothal refrigeration cyclopropane, and continuous caudal and continuous spinal methods. In regard to the latter he warns that most of the enthusiasts are the surgeons who exult in the unlimited time given them and he questions the wisdom of 6 and 7 hour operations with these methods.

There is an excellent chapter on the hazard in anesthesia, and one titled *Our Wives and our Children—Who Shall Anesthetize Them?* which leads to the suggestion that the anesthetist consider his patient as he would a member of his own family in the same situation. While this is laudable, of course, the chapter might easily have been shortened or left out altogether.

The new edition is valuable not only because it brings the book up to date, but because it avoids worthless controversial discussion and spends its time on instructive technique and good advice from Dr Flagg.

THOMAS H. COLEMAN

THE second English edition (last German edition appearing in 1926) of Zondek's *The Diseases of the Endocrine Glands*² is certainly of value to the advanced student of endocrinology. The bibliographical material and the theoretical discussion are as usual of interest. The fundamental chemical and physiological work both from a historical point of view and from a didactic point of view is well presented. This edition however although coming into print in 1944 should be regarded as not quite up to date. Discussion of the function of the posterior pituitary for instance, fails to include any reference to or mention of the work of Steven Ran- som discussion of the male hormone testosterone physiologically and clinically does not mention its most fundamental and important action that of storing nitrogen in the somatic muscular system a discussion of the thyroid diseases does not include any reference to goitrogenic substances such as thiouracil. Despite these defects this classic text book remains a source of stimulation and valuable ideas.

M. P. STARR

IT is the author's purpose in *Operations of General Surgery*³ by Thomas G. Orr to accomplish the most difficult task of providing in one volume an operative surgery which contains the essential techniques in the field of general surgery. There can be no doubt but that Dr Orr has achieved his goal in a most admirable fashion.

The charm of the book lies in its simplicity of presentation of proved and established operative procedures of general surgery and of most of its

¹THE DISEASES OF THE ENDOCRINE GLANDS. By Hermann Zondek, M.D. (German). Translated by Carl P. Gilman, M.D. M. R. C. S. L. R. C. P. Baltimore: The Williams & Wilkins Co. 1944.
²OPERATIONS OF GENERAL SURGERY. By Thomas G. Orr, M.D. Philadelphia and London: W. B. Saunders Co. 1944.

³THE ART OF ANESTHESIA. By Paul J. Flagg, M.D. 7th ed. Philadelphia, London, and Montreal: J. B. Lippincott Co. 1944.

specialties. Illustrations are profusely employed in a step-by-step manner leaving little to be desired.

It is not the purpose of the book to discuss preoperative and postoperative treatment or surgical pathology. Wherever necessary, however, there is a brief but adequate description of the anatomy of the region under consideration, and this is followed by a discussion of the dangers inherent in the procedure about to be undertaken. The techniques employed

for each operation are discussed and when common disease is encountered, usually more than one approach is presented.

It is amazing that such a enormous amount of material can be covered in one volume. There is no space devoted to nonimportant information. For the general surgeon or the student, this book serves for a quick and satisfactory reference.

HARRY P. JEWELL

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ESSENTIALS OF ALLERGY. By Leo H. Crip, M.D. With foreword by Robert A. Cooke, M.D. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1945.

POET-PRYCEMANS AN VYTHOLOO OF MEDICAL POETRY WRITTEN BY PHYSICIANS. Compiled by Mary Lou McDonough. Springfield, Ill.: Charles C. Thomas, 1945.

TRANSACTIONS OF THE AMERICAN NEUROLOGICAL ASSOCIATION. Seventieth Annual Meeting Held at the Waldorf Astoria, New York, May 9 and 10, 1944. Richmond, Virginia: The William Byrd Press, Inc., 1945.

IMPROVED LABORATORY TECHNIQUE. CLINICAL PATHOLOGY, BACTERIOLOGICAL, MYCOLOGICAL, VIROLOGICAL, PARASITOLOGICAL, SEROLOGICAL, BIOCHEMICAL AND HISTOLOGICAL. By John A. Kohner, M.S., M.D., Dr. P.H., Sc.D., LL.D., L.H.D., F.A.C.P., and Fred Boettner, V.M.D. 4th ed. New York and London: D. Appleton Century Co. Inc., 1945.

ANATOMY AS BASIS FOR MEDICAL AND DENTAL PRACTICE. By Donald Mainland, M.B., Ch.B., D.Sc., F.R.S.E., F.R.S.C. New York and London: Paul B. Hoeber Inc., 1945.

STUDIES OF BURNS AND SCALDS (Reports of the Burns Unit, Royal Infirmary, Glasgow, 1942-43). General Introduction, by L. Colebrook. Part I, by L. C. Colebrook, T. Gibson, and J. P. Todd; Part II, by L. C. Colebrook, A. M. Clark, T. Gibson, and J. P. Todd; Part III, by T. Gibson and A. Brown; Part IV, by A. Brown; Part V, by A. B. Anderson; Part VI, by T. Gibson with Appendices

Medical Research Council Special Report Series No. 249. London: His Majesty's Stationery Office, 1944.

LA RADIOLOGIA EN EL ESTUDIO DE LA VESICULA BILIAR. By Pedro A. Barcia. Buenos Aires: Libreria y Editorial El Ateneo, 1945.

LA RADIOLOGIA EN LOS DOLORIS LUMBARES Y CERVICIS. By Dr. Mario A. Caminoni. Buenos Aires: Libreria y Editorial El Ateneo, 1945.

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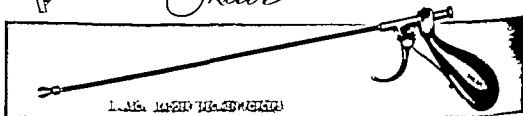
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GYNECOLOGY AND OBSTETRICS

An International Magazine, Published Monthly

VOLUME 80

JUNE, 1945

NUMBER 6

THE MECHANISM OF SHOCK FROM BURNS AND TRAUMA TRACED WITH RADIOSODIUM

CHARLES L. FOX, Jr. M.D. and ALBERT S. KESTON M.D. Ph.D. New York, New York

IN studies of shock emphasis has recently shifted from the plasma proteins and other colloids to the electrolytes. Rosenthal demonstrated that in standardized shock from burns or trauma sodium salts in isotonic solution are as effective as equal volumes of serum and showed that the curative effects of serum are due to its electrolyte content. (20) Clinical studies in shock caused by extensive thermal burns demonstrated the therapeutic efficacy of large doses of sodium salts in isotonic solution and led to the discovery of an unexpectedly large sodium retention (7).

These investigations pointed to the existence of a heretofore unrecognized and possibly fundamental derangement in shock redistribution of sodium. Accordingly radioactive sodium (Na^{24})¹ was used to explore whatever changes might occur after shock from burns or trauma.

From the Departments of Bacteriology and Biochemistry, College of Physicians and Surgeons, Columbia University and the Department of Psychiatry, New York University, Bellevue Hospital.

Work done under terms of contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University. A preliminary report was presented at the 94th meeting of the American Society for Clinical Investigation.

Aided by grant from the Josiah Macy Jr. Foundation. The sodium isotope used in these experiments was prepared in the Radiation Laboratories of Columbia University and was kindly supplied by Dr. John R. Dunning. In accordance with conventional usage (8) the less cumbersome term radiosodium will be used hereafter to denote Na^{24} .

PROCEDURE

Two types of experiments were conducted, the technique of Rosenthal being used for production of standardized shock from burns and from trauma (20). In one type animals were prepared with radiosodium given in isotonic sodium chloride solution so that the body sodium was in equilibrium and tagged with the isotope. Shock was produced 20 hours later and the concentration of radio sodium in the tissues and organs was determined in the animals during shock but not *in extremis*. In a second type of experiment shock was produced first and the animals were then treated with isotonic saline containing some radiosodium. About 20 hours later upon recovery from potentially fatal shock (as judged by death of untreated controls) the concentration of radiosodium was determined in tissues and organs. The water content of all tissues sampled was also measured by drying the tissues at 110 degrees C for 18 to 24 hours. Similar analyses were performed in parallel control animals which had not been injured but had received equal doses of radioactive sodium.

Mice were used for these reasons: the burns produced by Rosenthal's technique are uniformly fatal

¹The Na^{24} was homogenized by wet sifting and radioactivity was measured with the Geiger-Müller counter. The procedure has been described in detail (3).

in untreated animals (94.6% mortality in 221 controls) and treatment with isotonic solutions of sodium salts is uniformly effective (6% mortality in 708 animals treated with 2.2 to 3 c.c. within 5 hours). Shock following application of tourniquets to both hind legs and release after 2 hours is also uniformly fatal (95.3% mortality in 127 controls). Therapy with isotonic solutions of sodium salts (or a protein-free ultrafiltrate of mouse serum) is uniformly effective—85% to 91% survived after the second injection in 200 mice (20). In a single experiment in this laboratory with 100 mice, results similar to those of Rosenthal were obtained. When other animals are used e.g. dogs, tourniquets must be applied for 5 to 10 hours and the occurrence of infection in the occluded extremities has complicated the "shock" that results (19).

RESULTS

The tissue analyses and plasma values are shown in Tables I and II. The radioactivity values are expressed as percentage of the dose injected per gram of fresh tissue. Thus if 1000 counts per minute of radioactivity (above background) were injected into a mouse and analysis of 1 gram of its tissue showed 10 counts per minute (above background) the activity of the tissue would be 1 per cent of the dose injected. The values for the extremity tissues are listed separately for hind legs and fore legs in all burn experiments in which only the hind legs were burned also in the experiments on traumatic shock in which tourniquets were applied to the hind legs only.

It is immediately apparent from Tables I and II that the concentration of radiosodium in the skin and muscles of the injured extremities was much greater than the concentrations in similar tissues in the uninjured extremities of the same animal or in normal control animals. There was also a less striking gain in water content in the tissues of the injured hind legs.

The studies of Gamble, Hastings and Eichelberger, Manery and Hastings, Manery and Bale, Peters and Harrison, Darrow and Yarnet have shown that most of the body sodium (except some in bone) is in the extracellular phase i.e. in the plasma and interstitial fluid. (The interstitial fluid is essentially an ultrafiltrate of plasma in equilibrium with plasma and containing little protein but nearly as much sodium.) Obviously the influx of plasma or interstitial fluid into tissues

causing a gain in water content (edema) will also increase the sodium content of the tissues. Accordingly the analytical values for radiosodium were examined in relation to the movement of these fluids and water. This was done by attempting to ascertain the distribution of sodium and water in the extracellular and intracellular phases of tissues by the formulas of Hastings and Eichelberger. The analytical values for radiosodium were utilized instead of gravimetric analyses by appropriate substitutions. Analogous data for normal animals have been reported by Manery and Bale.

The values for extracellular fluid are obtained by the following calculation¹

$$\frac{\text{Extracellular water (grams per kgm. (or "sodium space" in injured tissues))} \times \text{Tissue radioactivity (\% dose per gram)}}{\text{Plasma radioactivity (\% dose per gram)}} \times \frac{0.93}{0.97} \times 1000$$

In regions where the antisodium barrier may have been demolished the sodium concentration in the tissue fluid is unknown; the term sodium space is used, therefore, to denote the volume of fluid which would contain all the sodium present in the tissue in a concentration equal to the plasma sodium concentration.

An approximation of intracellular water was obtained by subtracting the above value for sodium space from the total water content. These data are shown in Tables I and II. Figure 1 a and b show the solids and extracellular and intracellular phases computed for muscle.

The calculation shows a great increase in the volume of "sodium space" in injured tissues and that this increase is far too large to represent a commensurate increase in the volume of extracellular fluid. Thus in some instances the intracellular phase by this calculation would appear to have vanished. It is apparent that the tissues have gained more sodium than water; that the normal sodium space (i.e. extracellular sodium) was infiltrated into the intracellular compartment indicating some demolition of the antisodium barrier. Thus in normal tissues the extracellular phase averaged 200 grams per kilogram and the

¹This computation has the additional advantage of giving values for sodium content which are independent of variations in serum radioactivity and permits comparisons of different experiments.

TABLE I — RADIOSODIUM AND WATER ANALYSES
ESTIMATION OF EXTRACELLULAR PHASE—
SODIUM SPACE —IN MUSCLE AND SKIN
IN NORMAL AND SHOCKED MICE PREPARED
WITH RADIOSODIUM 18 HOURS IN ADVANCE

Extremity	Muscle			Skin	
	Radio-activity (% dose/grm. tissue)	Water content (gm./kgm.)	Apparent extra-cellular phase sodium space (gm./kgm.)	Radio-activity (% dose/grm. tissue)	Water content (gm./kgm.)

Normal

(1)	(2)	(3)	(4)	(5)	(6)
Fore	0.60	740	—	403	583
Hind	907	733	—	37	556
A (Serum)	—				
Fore	665	734	94	71	55
Hind	876	728	108	74	53
B (Serum)	3.2				
Fore	671	741	53	93	514
Hind	667	733	53	67	56
C (Serum)	4.1				

Burn (of hind legs only)

Fore	78	740	97	18	603
Hind	705	770	430	2.7	670
D (Serum)	2.81				
Fore	846	76	—	2.13	30
Hind	876	703	—	3.34	764
E (Serum)	—				
Fore	1.108	706	3	2.32	604
Hind	1.68	743	3.5	3.15	604
F (Serum)	3.1				

Tourniquet (to hind legs only)

Fore	97	730	30	2.46	554
Hind	3.02	76	678	2.	6.5
G (Serum)	4.31				
Fore	745	736	67	98	570
Hind	2.15	79	256	2.78	654
H. (Serum)	4.4				
Fore	663	713	30	613	606
Hind	87	706	330	3.9	754
L (Serum)	3.1				

TABLE II — RADIOSODIUM AND WATER ANALYSES ESTIMATIONS OF EXTRACELLULAR PHASE — SODIUM SPACE — IN MUSCLE AND SKIN IN NORMAL AND SHOCKED MICE 20 HOURS AFTER THERAPY WITH RADIO-ACTIVE 0.9 PER CENT SODIUM CHLORIDE

Extremity	Muscle			Skin	
	Radio-activity (% dose/grm. tissue)	Water content (gm./kgm.)	Sodium space (extra-cellular phase) (gm./kgm.)	Radio-activity (% dose/grm. tissue)	Water content (gm./kgm.)

Normal

(1)	(2)	(3)	(4)	(5)	(6)
Fore	9	7	4	75	6
Hind	0.5	746	7	5	630
M (Serum)	5.1				
Fore	54	770	30	05	300
Hind	553	770	7	—	480
N (Serum)	4.				
Fore	—	—	—	—	—
Hind	8	700	90	78	505
O (Serum)	3.0				

Burn

Hind	05	774	313	4.4	770
P (Serum)	6.31				
Hind	8	785	1.8	6.9	724
Q (Plasma)	8.451				

Tourniquet (to hind legs only)

Fore	7	7		5.6	535
Hind	3	8	830	9.60	770
R (Serum)	6.				
Fore	99	660		4.7	530
Hind	9.66	700	7.4	8.6	690
S (Serum)	12.1				
Fore		730	28	1.68	51
Hind	10.66	830	6	8.00	730
T (Serum)	6.1				

130 grams per kilogram of nonsodium containing intracellular phase!

In the treatment experiment furthermore the values for radiosodium excretion by all routes showed a marked retention of sodium in the shocked mice in the 24 hours after therapy. Similar retention had also been noted in the patients with extensive burns treated with isotonic solutions of sodium salts (7). Accord

intracellular phase about 530 grams per kilogram in injured tissues the apparent extra cellular phase or sodium space increased to 700 grams per kilogram leaving only about

TABLE III.—THE RETENTION OF RADIOSODIUM ADMINISTERED AFTER INJURY

Time of radioactivity count	Normal mice*	Burned mice*	Tourniquet mice*
Immediately after injection—hrs	00	00	00
44	47	8	97
48	14	16	76
7	<1	24†	
96		20†	30

Therapy consisted of single intraperitoneal injection of a volume of 0.9 per cent sodium chloride containing radiosodium equal to 6 per cent of body weight. The dose was given from 1 to 2 hours after injury.

Counts of 7 rays were made with the Geiger counter by placing the animal in fixed position before a 3.5 mm. thick lead shield to exclude β rays. Each value is an average of animals.

*The values are expressed in per cent of the amount of radioactivity in the animal immediately after injection.

†These values are much lower because legs and tails containing radiosodium sloughed off from some of the mice. Three of these mice died.

ingly this phenomenon was investigated further.

Shock was produced in groups of 10 mice by a standardized burn and by application and release of tourniquets on the hind legs (20). One hour later the injured mice which were in shock were treated with a dose of 0.9 per cent sodium chloride equal to 16 per cent of their body weight by a single intraperitoneal injection. A group of normal mice received a similar injection. The saline solution used contained radiosodium and the total radioactivity of each animal was measured immediately after the injection and at 24 hour intervals thereafter. Thus excretion of the dose of sodium chloride is indicated by decreased radioactivity of the animal as compared to its initial radioactivity.¹

The average values are shown in Table III and clearly demonstrate that in the first 24 hours the injured animals retained nearly all the sodium chloride injected. On the contrary the normal mice excreted over half the isotope and since mixing of isotope and body sodium occurs fairly rapidly (15) presumably some of their original sodium was excreted in addition. The sodium retention persisted in

TABLE IV.—COMPARISON OF EXPERIMENTAL VALUES WITH CALCULATED VALUES FOR 1 KILOGRAM OF NORMAL MUSCLE INFUSED WITH VARIOUS INCREMENTS OF PLASMA (OR INTERSTITIAL FLUID)

	Water content (gm./kgm. tissue)	Sodium content (mEq./kgm. tissue)	Sodium space (gm./kgm. tissue)
Found in normal muscle	730	52	72
Calculated for 1 gm. of normal muscle plus 30 of plasma	773	46	29
Found in muscle in burned mice	770	+56	+100
Calculated for 1 gm. of normal muscle plus 300 of plasma	804	61	46
Found in traumatized muscle in tourniquet shock	796	+100	+100
Calculated for 1 gm. normal muscle plus 200 of plasma	800	61	29

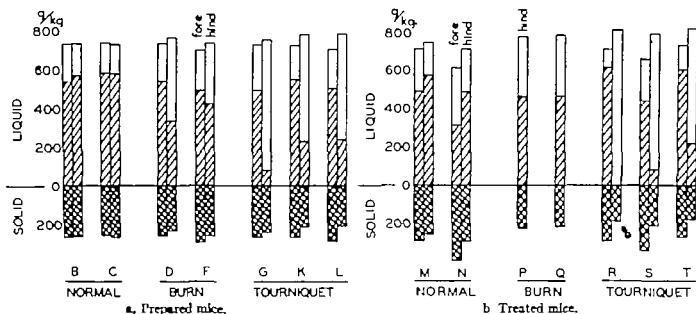
the injured animals 96 hours later these mice still contained more of the injected sodium than did the normal animals at 48 hours.

DISCUSSION

The experiments in prepared animals trace the movement of sodium and water in essentially normal untreated animals subjected to severe injury by burning or tourniquet trauma. The studies of Manery and Bale (15) and of Kaltner and associates indicate that equilibrium had been obtained between extracellular sodium and radiosodium in the 20 hours prior to injury hence movement of the isotope represents movement of sodium. In the therapeutic experiments, 20 to 24 hours elapsed from the time of injection of radiosodium to analysis (and the animals were in good condition at that time) so that substantial equilibrium had been established. Some parallel gravimetric sodium analyses of tissues support this interpretation (8).

The data in Tables I and II clearly show the massive shift of sodium into injured tissues; it is apparent from the water analyses that relatively much less fluid was transferred. The computation of tissue sodium space shown in Figure 1 a and b is based on the data of Hastings and associates (11, 14) which show that in tissues sodium is in a fluid in equilibrium with plasma i.e. containing a similar concentration of sodium. The very high sodium space in tissues computed

¹The possibility of failure of absorption of the isotope from the peritoneal cavity of mice in shock is excluded by the data in Tables I and II showing that isotope administered after injury is absorbed and distributed throughout the tissues.



a. Prepared mice.

b. Treated mice.

Fig. 1. Redistribution of sodium in injured muscles. In each pair of columns the left represents muscles of both un-injured forelegs and the right muscles of both injured hind legs of mice in Tables I and II with serum analyses. Clear space indicates "extracellular phase"—assuming that sodium in normal and traumatized tissue is extracellular; diagonal lines, intracellular water; cross hatch, solids. (All

measurements are expressed in grams per kilogram fresh muscle.)

In the injured tissues, the "extracellular phase" appears greatly increased with consequent diminution or disappearance of the intracellular compartment apparently the antisodium barrier was demolished and extracellular sodium moved into the cells.

from the present data shows definitely that much of the sodium is in tissues *without* a proportionate increase in fluid. It appears that much of the tissue water has taken on this property of extracellular fluid that is that much of the sodium had become located within the cells. (Subsequent data (8) on potassium loss indicate an exchange of sodium for intracellular potassium.) Thus in traumatized tissues the conventional extracellular fluid space has been supplanted by a far larger sodium space composed of (a) extracellular edema fluid and (b) intracellular water containing excess sodium. In this way the sodium loss into a traumatized area far exceeds the fluid loss in relative and absolute values.¹

This excess of sodium loss may be clearly discerned in Table IV which shows the extracellular fluid volumes computed if 250 cubic centimeters 500 cubic centimeters or even 1000 cubic centimeters of plasma (or interstitial fluid) infiltrated into the extracellular compartment of 1000 grams of fresh muscle. The great influx of sodium after trauma may be appreciated when it is realized that a kilo-

gram of muscle saturated with a liter of plasma would contain less sodium but more water than was found in our analyses of traumatized muscle.

The significance of the marked retention of therapeutically administered sodium becomes apparent when considered in relation to these tissue analyses. As a consequence of the sodium and fluid loss in the injured tissues the extracellular compartments elsewhere in the body are depleted. The electrolyte and fluid redistribution is similar to that found by Darrow and Yannet in their experiments in which sodium was removed without loss of fluid. After injury moreover there is the added factor of extracellular fluid immobilized as edema in the injured area. Consequently as much as half the total extracellular sodium in the body may have been removed from active circulation.² Accordingly after administration of large amounts of isotonic solutions of sodium salts to the animal in shock the deficit in available extracellular fluid is made up and only sodium in excess is

(1) It is noteworthy that although the amount of available extracellular sodium has been greatly reduced, no sodium has been removed from the body. Hence measurements of extracellular fluid volume by radio-sodium show no change whatever as normal amounts of sodium ions are still present. (2) In the hypotonic area equilibrium is reached prior to therapy (8) when the plasma sodium concentration is substantially unchanged.

W. are radiated. Dr. Ed. B. H. Quinby for the use of her portable counter. For details measurements of radio-sodium in human burns. These indicated gross influx of sodium into burned tissues (8).

excreted. Thus little or no sodium is excreted in the urine by the severely injured animal (or patient) whereas most of the sodium given is promptly excreted by normals. When the amount of solution administered exceeds the volume of extracellular fluid depleted, the excess is excreted; this occurred when the injury was less extensive or the amount of solution exceeded 15 per cent of body weight that is half the total extracellular volume.

Wiggers has stated that reduction in the volume of blood returned to the heart is the keystone of all modern conceptions of shock. Extensive clinical studies (4) have shown that in human cases of shock, circulatory failure results from inadequate blood return to the heart because of the marked reduction in plasma volume. Decisive information as to the cause of this decrease in plasma volume is relatively meager and the belief that plasma is 'lost' into injured tissues is based on indirect evidence. For example, Beard and Black analyzed fluid obtained by centrifuging excised portions of injured tissues and found its protein content approximated and sometimes exceeded that of the plasma. On this basis they inferred that this fluid escaped from blood vessels at the sites of injury and in their paper 'Reasons are given for believing that the loss of plasma proteins at the site of injury is the most important factor in the production of shock.' Since tissues normally contain three times as much protein as plasma, the occurrence of proteins in tissue fluid does not necessarily prove their source is the plasma. More recent tissue analyses (8) fail to demonstrate an increase in proteins at the sites of injury and indicate instead that the proteins in the fluid from injured tissues came from the injured tissue cells themselves (17). Another example of the inadequacy of the local plasma loss hypothesis is the report of Fine and Seligman that although a traumatized extremity of a dog gained 69 grams in weight, the plasma 'loss' in the animal was 700 cubic centimeters—a tenfold discrepancy.

Gamble has emphasized the unity of electrolyte structure of extracellular fluid composed of the plasma of the blood and the interstitial fluid (including lymph) which lies

between the vascular compartment and the tissue cells. Furthermore there is clear evidence (5, 8, 12, 16) that the volume of circulating plasma is in large part dependent upon the volume of extracellular fluid and its concentration of sodium. The mechanism which determines the relative size of the two fractions of extracellular fluid is not understood. Hopper, Elsdon and Winkler found that after equivalent reduction of extracellular fluid by (a) prolonged water deprivation and by (b) rapid salt depletion there was a disproportionately greater reduction in plasma volume after (b) removal of sodium.

The present experiments demonstrate the very great accumulation and side tracking of sodium in injured tissues with subsequent reduction in plasma volume characteristic of traumatic shock. Conversely treatment with an amount of isotonic sodium solution approximating one-half the extracellular volume restored this volume. On this basis, the successful treatment of shock in animals (20) and a man (7) with large volumes of isotonic solutions of sodium salts is explained.

SUMMARY

Radioactive sodium was used in mice to compare the sodium content of normal tissues and those injured by burning or by tourniquet trauma.

The sodium content of injured skin and muscle is greatly increased and exceeded the gain in water (edema). This indicated that additional sodium accumulated in the intracellular compartment.

As a result of the redistribution of sodium and water approximately one-half the total amount of extracellular sodium was side-tracked and rendered unavailable. Administration of this amount of sodium by injection of 0.9 per cent sodium chloride containing radiosodium was followed by nearly complete retention of sodium in the injured animals but by excretion of sodium in normals.

The relationship between the reduction in plasma volume characteristic of shock and depletion of extracellular fluid is discussed.

The extensive and thorough biochemical studies of Taylor and Rosenthal have just appeared in *Public Health Reports* April 6 and 3, 945, 60, 378-38, 40-42. The close similarity of their data and ours is noteworthy.

It is encouraging to note that the latest recommendations (*Shock Report No. 57*) of the Subcommittee on Shock of the National Research Council for the treatment of extensive burns state "Replacement therapy in the first 48 hours thus involves fluid volumes of these magnitudes, totally 8000 to 15,000 c.c. for the 48 hour period."

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AN ANALYSIS OF THE MASSACHUSETTS GENERAL HOSPITAL CASES OF LUNG ABSCESS FROM 1938 THROUGH 1942

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THE last report on lung abscess from the Massachusetts General Hospital showed evidence of improvement in the results of treatment during the 5 year period 1933 through 1937 as compared with those of earlier reports (2). Sufficient time has now elapsed to include a 2 year period of follow up after the next year period 1938 through 1942 and this report is offered for comparison with that of the preceding 5 year period.

Chart 1 gives a comparison of our experience with lung abscess arranged in periods the first of 8 years (1) the second of 5 years (2) and the third of 5 years. Over the total period of 18 years covered by these three groups there has been a progressive rise in the number of patients cured and a corresponding drop in the number of patients who have died of the disease. There has been a less striking drop in the number of patients who remain alive with disease. These trends were particularly noticeable during the period 1933 through 1937 and were ascribed to certain factors such as improvement in the technique of the drainage operation more prompt application of surgical treatment and particularly the utilization of lobectomy when the case was thought to be unsuitable for drainage or when drainage alone had failed to effect a cure. It was pointed out also that all other types of operation such as thoracoplasty redrainage after failure of the drainage procedure and plastic procedures for closure of chronic cavities were unsuccessful. As a result of this experience these procedures were abandoned and during the next 5 year period reported upon here (1938 to 1942) the only surgical operations used were drainage and lobectomy either primary or secondary.

In the present series 120 cases are reported. Chart 2 gives an analysis of the outcome of

these 120 cases. Seventy-one (59.2 per cent) were cured. Of these there were 28 spontaneous or nonoperative cures (23.3 per cent of the entire group) and 43 cures resulting from operation (drainage primary lobectomy or lobectomy after drainage had failed to cure). Twenty-two patients died (18.3 per cent). Of these 11 died without operation and 11 died after operation. The remaining 27 patients (22.5 per cent) survived but were not cured. Six of these were not operated upon. Twenty-one were drained but the operation did not result in cure and for one reason or another no subsequent lobectomy was carried out.

ANALYSIS OF THE 75 CASES OF PATIENTS WHO WERE OPERATED UPON

Seventy-five patients were subjected to operation either primary lobectomy or drainage (Chart 3). In the latter group the only secondary operation resorted to in any case was lobectomy or pneumonectomy.

Primary Lobectomy Cases

In 15 cases (20 per cent) a primary lobectomy was performed. The reasons for choosing this operation were as follows: chronicity of the disease 10 cases hemorrhage 2 cases more than 1 lobe involved 1 case mistaken diagnosis of carcinoma 1 case abscess located in upper lobe 1 case. The most frequent indication was the chronicity of the case. It was observed in the last report as a result of a careful study of the duration of disease in each case that no patient whose abscess had existed for 1 year or over recovered without surgery and that very few cases of such long standing responded to drainage alone. Of the 15 cases in the present series only 5 were of less than 1 year's duration. Three had been going 1 to 2 years 3 had existed 2 to 5 years and 2 were known to have existed longer than 5 years. In 2 cases the duration was not known.

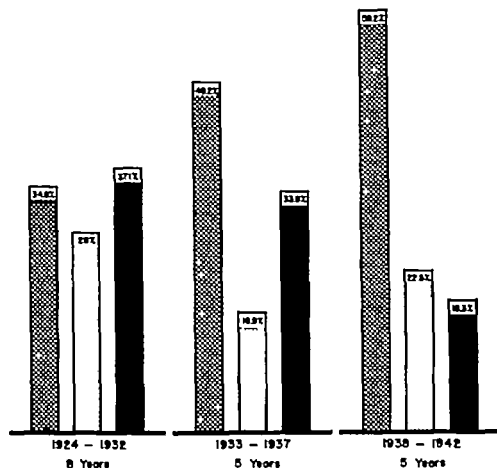


Chart 1. Comparison of experience with lung abscess at the Massachusetts General Hospital during 3 periods of observation. Dark dots indicate cured light dots, alive with disease and black areas deaths.

Serious hemorrhage led to the choice of lobectomy in 2 cases because experience has shown that massive hemorrhage is one of the important causes of death in cases of lung abscess. It may occur after drainage as well as before and packing cannot be relied upon to stop it.

The location (right upper lobe) or extent of the disease led to the choice of lobectomy in two cases and in one case the preliminary diagnosis was carcinoma. In this case however the lesion was found on exploration to be a lung abscess and a lobectomy was performed.

Technique One of the characteristics of lung abscess is that it is associated with an immense hyperplasia of the hilar lymph nodes and marked inflammatory induration of all adjacent structures including the tissues surrounding the pulmonary vessels. Because of this it was impossible to carry out a dissection and separate ligation of these vessels in 10 of

the 15 cases and the tourniquet method of dealing with the structures at the hilum had to be used.

Postoperative course Of the 10 patients in whom the tourniquet technique was used 2 died of sepsis (spreading pneumonitis in one and subphrenic abscess and peritonitis in the other). Of the 8 survivals in this group an empyema developed in 6. In only 3 of these was adequate chemotherapy used. In the remaining 2 patients primary healing resulted. These both had chemotherapy.

In the 5 patients who had individual ligation and separate bronchial closure using silk technique throughout there were 4 uncomplicated recoveries and 1 case of empyema. The latter case was the only one of the five in which sulfa drugs were not used.

In all the cases of empyema following both types of technique recovery was complete though delayed. All patients in this group remain cured.

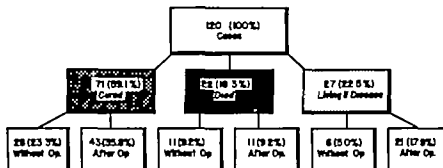


Chart 2. Total experience with 120 cases of lung abscess, including all methods of treatment.

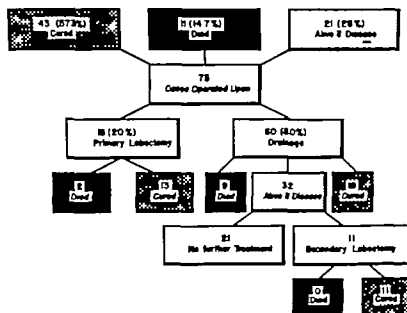


Chart 3. Results of surgical treatment in 75 cases of lung abscess.

In the last previously reported series of 125 cases (1933 to 1937) primary lobectomy was employed in 6 patients, 1 of whom died. The ratio of postoperative deaths is approximately the same in the present group and, if both are added together making 21 cases of primary lobectomy with 3 deaths in all, we find a postoperative mortality of approximately 1 of 7 patients operated upon.

Drainage Cases

In the remaining 60 cases drainage of the abscess was performed. The method described in the last report (2) was followed without modification. In 15 cases a one stage

procedure was used while in 45 cases the two stage operation was performed.

The results of drainage in these 60 cases, like those of the last reported series, were disappointing in spite of the fact that the great majority of the patients were operated upon soon after they were admitted to the hospital. Chart 4 shows that of the entire group of 75 patients treated surgically 40 were operated upon within the first 2 weeks and 61 within the first month after entry. As a result of drainage 19 patients were cured, 9 died, and 32 are classified as alive with disease. The last group includes those with a persistent cavity or bronchocutaneous fistula. Eleven of these

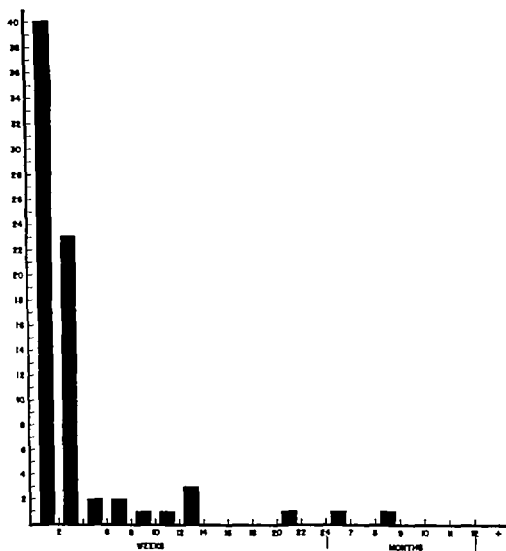


Chart 4. Elapse of time between date of entry to hospital and date of operation.

patients were cured subsequently by secondary lobectomy or pneumonectomy. There were no deaths following this procedure.

As before the criteria of cure were freedom from cough and expectoration, disappearance of abnormal physical signs and x ray evidence of complete healing.

Causes of death after drainage operation. As is characteristic of any series of lung abscess cases the most frequent cause of death after the drainage of the abscess was spreading infection in the lung. This occurred in 5 cases. Massive hemorrhage was responsible for 2 deaths and brain abscess for one death. The only postoperative fatality which can properly be ascribed to the surgical procedure was the one patient who died suddenly while on the operating table. In spite of a definite rule of the thoracic service that all patients with

lung abscess must be operated upon with the head lower than the feet, the operation in this case was carried out in the sitting position. On incision of the lung there was a sudden collapse resulting in coma followed promptly by death which was attributed to cerebral air embolism. This fatality must therefore be ascribed to technical error.

The *postoperative mortality* of the drainage operation in this series, inasmuch as all but 1 patient died of the progression of his disease is therefore 1 in 60 cases, or 1.7 per cent.

Lobectomy After Failure of Drainage to Cure

In the majority of patients who had persistent disease following drainage a lobectomy was advised. The operation was carried out in 11 of these. Analysis of the reasons for not operating upon the 21 others reveals that 8

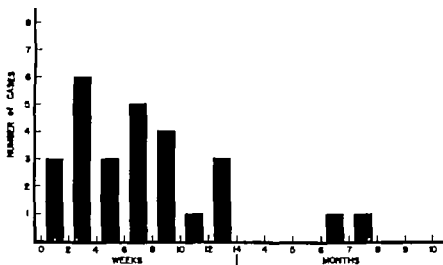


Chart 5. Spontaneous cure cases: elapse of time from onset of disease to date of entry to hospital.

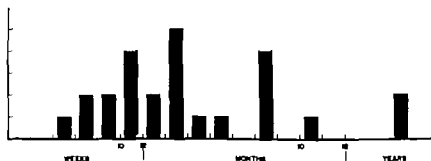


Chart 6. Spontaneous cure cases: elapse of time from date of onset to date of proved cure.

patients were working full time and were unwilling to give up their jobs. Four patients stated that they had so few symptoms that they were satisfied to remain as they were. In 1 case an attempt was made to perform a lobectomy, but the operation was abandoned because of technical difficulties arising from widespread vascular adhesions. The proportion of secondary lobectomy operations carried out would no doubt be greater during a period of more unemployment than existed from 1937 to 1942.

Of the 11 patients operated upon none died. All were cured. In 2 cases there was primary healing. In these the operation was carried out by the vessel ligation-bronchus suture technique, silk being used. In all the others there was a complicating empyema which ultimately healed. The tourniquet method

was used in all of these but 2, and in these 2 cases chronic catgut mattress sutures were used. This method of bronchial closure has since been given up and supplanted by the use of fine silk sutures over the end of the bronchial stump (method to be reported).

ANALYSIS OF THE 45 CASES OF PATIENTS WHO WERE NOT OPERATED UPON

Of the 45 patients who were not operated upon 28 recovered spontaneously, 11 died, and 6 remained alive with disease because they refused operation. The causes of death in the group of 11 patients who died were overwhelming infection in 6, brain abscess in 4, and complicating ulcerative colitis in 1. Operation was not advised in this group because of the fact that these patients were all hopelessly ill. Two died in less than 24 hours after arrival.

Twenty-eight patients recovered without surgery (23.3 per cent of the entire group). That there was not an unusually large percentage of very early cases is shown in Chart 5 which illustrates the duration of the disease from its onset to the date of entry of the patient to the hospital. It is interesting how ever that in the majority of these cases the disease was of $3\frac{1}{2}$ months duration or less. A more important fact is demonstrated by Chart 6 which shows that the total duration of the disease in many of the spontaneous cure group was of surprising length. Although 9 patients recovered in 3 months or less there were 8 in whom the disease lasted 3 to 6 months and in 6 patients from 6 to 12 months. Two patients recovered after the expiration of 1 year.

The usual symptomatic treatment, bed rest, and postural drainage were employed in this group. In only 5 was adequate sulfa drug chemotherapy used.

SUMMARY OF ANALYSES

This group of lung abscess cases represents the latest of a series of reports from the Massachusetts General Hospital dealing with this disease. It brings to 681 the total number of cases reported from this hospital.

Table I gives a comparison of the results in each of the last 3 groups. Certain interesting observations can be made from it. First there has been a definite increase in the total number of cures by all methods of treatment. The present figure is 59.2 per cent as compared with 49.2 per cent for the last series and 34.8 for the one before that. There was a corresponding fall in the number of deaths, the present figure being 18.3 per cent as compared with 33.9 per cent in the last series reported. This represents a much more pronounced drop in mortality than occurred between the last two reports. The percentage of spontaneous cures remains approximately the same—23.3 per cent.

There was a further drop in the operative mortality after the drainage procedure to 1.6 per cent. This is in line with the experience of other clinics. The percentage of cures resulting from surgery continues to increase reaching a figure of 35.8 per cent of the entire group.

TABLE I.—COMPARISON OF RESULTS OF PRESENT GROUP WITH PREVIOUSLY REPORTED SERIES

	924-03 Per cent	913-1017 Per cent	918-101 Per cent
Cured	34.8	49.2	59.2
Died	37.1	33.9	18.3
Alive with disease	18.0	16.9	21.5
Cured spontaneously	21.4	19.3	23.3
Cured by surgery	12.8	29.9	35.8
Operative mortality (drainage cases)	12.5	7.4	1.6
Number of patients operated upon	45.7	68.5	64.8

TABLE II.—USE OF SULFA DRUG CHEMOTHERAPY

	N of cases	N receiving sulfa drugs	Percentage
Entire series	120	43	35.8
Those cured	71	21	29.5
Those who died	22	6	27.3

of 120 cases. On the other hand there was no significant change in the percentage of patients operated upon. There was a relative increase however in the number of patients on whom a primary lobectomy was performed. Of this group there were 15 cases as compared with 6 in the last series and none at any time before that.

Influence of sulfa drug medication. Sulfa drug chemotherapy began to be used during the period covered by this last series. The possible influence of the use of these drugs in increasing the percentage of cures and decreasing the percentage of deaths must be considered. The administration of one of these chemotherapeutic agents in adequate dosage was carried out in 43 or 35.8 per cent of the entire group of 120 cases. The total number of patients who recovered as a result of all forms of treatment was 71. Of this group 21 received sulfa drug therapy. Therefore 29.5 per cent of those who recovered received these drugs. Of the entire series 2 died and 6 of these patients were treated with sulfa drugs making 2.3 per cent. It is obvious that there is no significant difference in these figures. One is forced to conclude therefore that the use of sulfa drug chemotherapy made no material change in the results in this series. Table II summarizes these data.

CONCLUSIONS

Although lung abscess continues to be a serious disease there has occurred over the

past 10 or more years an encouraging increase in the number of cures and a gratifying reduction in the mortality rate. That this improvement in the results of treatment is probably not due to the influence of the administration of sulfa drug chemotherapeutic agents is strongly suggested by the data presented. The improved results if not due to a diminution in the virulence of the infection in the average case are most likely accounted for by

a greater knowledge of the disease and a better understanding of the principles of treatment. The fact that the management of these cases in the Massachusetts General Hospital has for many years been the responsibility of a very small group may be of significance.

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POSTOPERATIVE PROPHYLAXIS OF RECURRENT MAMMARY CANCER WITH TESTOSTERONE PROPIONATE

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THE effect of hormones upon the production growth and treatment of cancer has been studied by innumerable laboratory and clinical workers. Recently these investigations have culminated in the important results obtained in patients with cancer of the prostate by castration and the subsequent use of synthetic estrogenic hormones.

ENDOCRINE DYSPLASIAS OF THE BREAST

In women the breast is undoubtedly one of the most hormone-sensitive organs. Certain changes of the breast, whether transient or chronic in character have been described under different names and are considered today by various investigators as functional or endocrine mastopathy. On this basis the following mastopathies can be grouped together: Cheate and Cutler's mazoplasia, Reclus cystic disease, Schimmelbusch's cystic adenoma, Aschoff's mastopathia chronica fibrosa cystica, and numerous other syndromes.

Semb pointed to the high incidence of cancer in cases of fibrous cystic mastitis which he called fibro-adenomatosis cystica mammae. Many workers before him however had suggested that inflammatory breast disease might have a tendency toward becoming malignant.

On the basis of the work of Cotte, Pallot and Berard (which in turn is based on earlier research of Leriche and of Wanke and Paulsen of Dahl Iversen and of many others) estrogens began to be used in the years 1935 to 1937 not only in cases of simple painful breasts, but also in cases of Reclus and Schimmelbusch disease. There were some favorable reports on this therapy, but results varied greatly and even were disastrous in some cases. I saw 1 successful case and 10 failures.

Further research disclosed the reason for these varying results. Functional mastopathy results from a disturbance of the hormonal

balance which may have various causes. Benzon recently classified mastopathies according to the etiology involved, as follows: (1) excessive blood estrogen, (2) excessive luteal hormone in the blood, (3) ovarian insufficiency, (4) of thyroid origin, (5) of pituitary origin, (6) of other origin. He estimates that about 50 per cent of cases of mastopathy are caused by hyperestrinism. In my opinion, this percentage is even larger because it would seem that the amount of estrogenic hormone fixed by the mammary glands should be taken into consideration as well as the estrogen level of the blood. The presence of a larger amount of estrogen in the mammary glands depends on the ability of this organ to store the hormone in a way which is not strictly related to the amount in circulation. It is obvious that in the case of hyperestrinemia, the mammae are likely to contain an excessive amount of hormone. Be this as it may, the failure of the treatment of mastopathy with estrogen is understandable.

The fibrous cystic mastitis which occurs in rats after estrogen treatment casts new light on this question. Incidentally the same condition has been observed in both men and women. This confirmed the important rôle estrogen plays in the production of mastopathy. I had the opportunity of seeing two women with mastopathy undoubtedly caused by excessive estrogen therapy. In 1937 I made the same observation in the case of a man 49 years of age suffering from a stomach ulcer who had received estrogen treatment for 6 months. This treatment resulted in mammary hypertrophy necessitating surgical intervention. Histologic examination showed fibrous cystic mastitis in both glands. The influence of the estrogenic hormone on mastopathy can often be proved by estrogen in the particularly large cysts seen in this disorder.

The use of the antagonistic hormone testosterone gives extraordinary results in most

cases of mastopathy. This therapy was only started in 1937 following the papers of Desmarest and Capitan (22-23) which are based on findings in 17 cases.

In 1938 I started to use testosterone propionate in the treatment of mastopathy and observed that 85 per cent of the patients reacted favorably not only as far as the pains in the breasts were concerned but also with regard to the hardening of the glands. There were no large cysts or papillomatous proliferations (patient with such conditions were operated upon). In the remaining 20 per cent no improvement occurred. After having treated 45 patients in this way I am convinced that the estrogenic hormone is not always responsible for the disorder. Since I have adopted the classification of Benzadon the results have improved.

MASTOPATHY AND CANCER

Many clinicians have described the development of cancer in cases of mastopathy. However they do not agree on the percentage in which this occurs. Semb reported a 24 per cent incidence of cancer in cases of cystic papillomatous mastopathy. Cheatle and Cutler estimate that 20 per cent of the cases of mammary cancer have their origin in mastopathy whereas Ewing reports 50 per cent.

Besides Semb's monograph 2 other fundamental investigations have been published on this subject one by Lindgren the other by Korpassy.

Lindgren calls attention to the confusion existing regarding the nomenclature. In agreement with the majority of other authors stating that most women are subject to mastopathy he finds such mammary changes very common as shown by his statistics on 60 autopsies of women between the ages of 35 and 75 years. However he encountered only 8 cases of pronounced epithelial proliferation.

Korpassy found at autopsy pathological changes in the mammary glands in two-thirds of a group of 300 women between 14 and 89 years of age. He found epithelial hyperplasia in 154 mammary glands, typical papillomas in 10 and cancer in 2.

Semb has stated that cancer develops particularly in cases of cystic papillomatous mas-

topathy but this does not exclude its occasional occurrence in other forms of mastopathy.

Recently (1944) Cole and Rossiter classified the various types of mastopathy (chronic mastitis) and added since we have observed carcinoma develop in areas of precancerous hyperplasia and have encountered this type of lesion in 15 or 20 per cent of our cases of carcinoma of the breast we are convinced that there is a definite relationship between carcinoma and chronic cystic mastitis, particularly in the type which we have described as precancerous hyperplasia.

My opinion (38-39) is similar to that of these writers. On the basis of studies of 11 cases of mastopathy in which I performed plastic amputation 12 biopsies and 7 cases of cancer which were accompanied by mastopathy (86 per cent) I believe that Cole and Rossiter's classification adequately set forth the present opinion with regard to the relationship between mastopathy and cancer. In 4 out of the 15 patients with mastopathy who underwent operation cancer was present. A particularly interesting case among them was that of a woman 26 years of age who had a tumor of several months duration located in the uppermost part of the left breast. Palpation verified the presence of a hardened zone which showed only a slight degree of opacity on transillumination. Special attention was given because even though a diagnosis of chronic mastitis had been made, there were two pea-sized nodes in the corresponding axilla. A biopsy was made with extirpation of the mammary tissue and removal of one of the lymph nodes. Histologic examination revealed chronic cystic mastitis with increased epithelial hyperplasia. Examination of the axillary nodes revealed metastases of solid carcinoma. Radical operation was performed and when the removed tissue was carefully examined a single nucleus of solid carcinoma smaller than a bean was revealed.

In my opinion the existence of mastopathy of the papillomatous type or the detection of papilloma as revealed by transillumination suffice to warrant suspicion of a malignant tumor whether the breast is bleeding or not.

¹The operation consists of the amputation of the mammary gland followed by transplantation of adipose tissue of the abdomen and by covering of the nipple so that an esthetic reconstruction is accomplished.

The other forms of mastopathy cannot actually be considered as precancerous although they do not exclude the possibility of cancer.

Accepting Cole and Rossiter's statement as a fact that 20 to 30 per cent of cases of mastopathy are of the precancerous hyperplasia type the real relationship between cancer and mastopathy can be estimated. Recently Warren studied 1,044 cases and states that cancer occurs 4 to 5 times more often in individuals with mastopathy than in healthy women. In his recent book Geschickter devotes a long chapter to the relationship between chronic cystic mastitis and cancer and cites the following points in support of the tenet of the existence of a causal relationship between mammary dysplasia and cancer:

1. In many cases breasts removed for cancer show the changes of some form of chronic cystic mastitis either grossly or microscopically.
2. Transitional stages between the two conditions have been traced by histologic investigation.
3. In the experimental production of mammary cancer in mice, using estrogenic hormones mammary changes resembling those found in cystic disease and adenosis precede the cancerous changes.
4. Among patients treated conservatively for mammary dysplasia a number develop mammary cancer subsequently.

Studying my cases with these points in mind I became convinced of the evident relationship between the two afflictions:

1. In 88 cases of mammary cancer a microscopic examination of the histologic specimens revealed mastopathy in 6 cases, or 6.8 per cent.
2. In 6 cases of mastopathy with pronounced epithelial hyperplasia, the diagnosis was very difficult because there were borderline tumors, and cancer was diagnosed in 4 cases, one of which was confirmed by the existence of axillary metastases.
3. There is no fundamental argument against the assumption that the spontaneous development of cancer in human beings goes through the same process as does experimental cancer in rats.
4. In 1 case of simple mastopathy which was verified histologically cancer developed after 4 years.

My personal conviction therefore is that a causal relationship between cancer and certain cases of mastopathy exists and that estrogen is a causative factor in the development of cancer. If this is so it is logical that the occurrence of cancer is higher in cases of mastopathy because hyperestrinism exists in almost every instance in both diseases.

EXPERIMENTAL CANCER PRODUCED WITH ESTROGENS

In 1932 Lacassagne (31) produced experimental cancer of the mammae in rats by injecting estrogens. The changes in the mammary tissue are progressive with cyst formation and eventually epithelial proliferation which results in cancer. Lacassagne demonstrated the importance of the constitutional predisposition since in the strains most susceptible to cancer the initial changes started in the second month, formation of cysts occurred in the third and cancer developed in the fifth month while in the less susceptible strains there were no changes before the third month and cancer occurred only in the fifteenth month.

Numerous investigators have confirmed this observation. Burrows produced mammary cancer in 2 male rats by applying estrone to the skin. Lewis and Geschickter according to Benzadon found that an extract of cancerous mammae of women contains considerable amounts of estrogen (6 rat units per gram).

The use of estrogens as a carcinogenic agent has become routine and some laboratories use such material for the production of experimental mammary cancer. Cook and associates list estrone with the carcinogenic substances. Moreover the entire chemical group of phenanthrene compounds is considered carcinogenic and it is known that this grouping forms part of the chemical nucleus of the ovarian hormones.

In 1938 Lacassagne (32) published statistics covering his investigations carried on since 1932 on tumors produced experimentally with estrogens. He concluded that mammary cancer is produced by estrogens only in strains with a tendency to spontaneous cancer. However in such strains the normal incidence of cancer is increased and the disease seems to develop earlier than usual in both male and female animals.

Geschickter in reporting his experimental investigations states that the percentage of rats in which estrogenic mammary cancers develop varies but when the animals survive the required time the disease may be present in 100 per cent of the survivors under certain

experimental conditions. He used rats from a colony of more than 5 000 animals (mainly on a standard diet and inbred for a period of 7 years) in which spontaneous mammary cancer did not occur. He also found that the total dose required to produce mammary cancer is not influenced by the size of the daily dose but varies with the duration of estrogen action of different estrogen compounds and with the method of administration.

ESTROGENS AND HUMAN CANCER

After Lacassagne's experiments the question immediately arose as to whether or not estrogens used therapeutically could cause cancer. There are a very few cases on record in which this is with more or less certainty reported to have occurred after estrogen had been used especially in cases of mastopathy (1936 to 1937). It is difficult to arrive at definite conclusions in this respect. On the basis of the doses (total 10 to 20 mgrm.) used experimentally in rats for the production of cancer, tremendous doses would seemingly be required to produce a similar effect in human beings.

Recently we observed a case of mammary cancer in a woman 35 years of age who had been treated with estrogen continuously for 5 years (progynon 10 000 I U. three times a month). The possibility of a cancerogenic influence of the estrogenic hormone cannot be eliminated in this case. In some other cases of mammary cancer observed the women had been treated with estrogens too, but the doses used were too small to warrant ascribing any cancerogenic effect to the estrogens.

ANTAGONISM BETWEEN ESTROGENS AND TESTOSTERONE

In 1926 Steinach, Kun and Peczenik presented some evidence of an antagonism between estrogens and testosterone. Later Moore and Price postulated that this antagonism might result from an inhibitory action of the androgen upon the pituitary with a resultant diminution or cessation of the ovarian production of estrogen. This interpretation does not eliminate the possibility of an actual biologic antagonism and the fact that the action may be indirect does not detract from its possible therapeutic significance.

Lacassagne (33) used testosterone in animals in an attempt to prevent the production of cancer caused by simultaneously administered estrogen. In the beginning when using testosterone acetate in small doses he did not succeed. He resumed his experiments with testosterone propionate in a dose of 7 to 8 times that of the estrogen, giving doses of 2 milligrams per week continuously until the death of the animal. Out of 18 females which survived for a period of 1½ to 18 months, not one developed cancer. Several other investigators have since confirmed this antagonism between the two hormones. Peralta Ramos in 1939 demonstrated the antagonism between testosterone and estrogen in rabbits and arrived at the conclusion that 1 milligram of testosterone propionate is capable of neutralizing approximately 50 rat units of estrogen. Geschickter was unable to prevent the occurrence of mammary cancer in his experiments, probably because he used insufficient doses of testosterone. Recently Benzadon confirmed the antagonism clinically and experimentally.

TESTOSTERONE IN INOPERABLE AND RECURRENT CANCER

Testosterone has been used only recently in the treatment of human cancer and little literature on this subject has been published. Ulrich in 1939 reported 2 cases of mammary cancer in which he used testosterone acetate. In the first case besides a cancer of the left breast which had been diagnosed clinically and confirmed histologically, appreciable changes were found in the right breast, apparently indicative of cystic mastitis of a high degree. Moreover the pathologic examination of the removed left breast revealed that the cancer had developed on the lesions of chronic mastitis. This patient who had complained of severe pains in the right breast as well as in the right arm which had gradually become emaciated, improved in a sensational manner after the operation following 10 injections of 10 milligrams of testosterone acetate. Ulrich's second case is also most interesting. This was a case of cancer of the right breast infiltrating the whole organ and with axillary involvement (clinical diagnosis). In the other breast two well circumscribed tumors were found. Since

the patient also had a uterine myoma accompanied by hemorrhage hysterectomy and bilateral castration was performed. The mammary cancer was considered inoperable at the time. Upon treatment with 10 injections of testosterone acetate all the subjective symptoms disappeared and the right breast improved so much that it was considered operable.

In spite of the criticism that can be made with regard to these 2 cases, the fact remains that they are the first that called attention to this subject. Another paper was published by Loeser also in 1939 in which he reported recovery after the administration of 1500 milligrams of testosterone in 2 patients with supraclavicular recurrence of cancer after a previous operation for mammary cancer. In 1942 Farrow and Woodard reported the treatment of 33 patients with mammary cancer and bone metastases who responded to relatively small doses of testosterone—5 to 10 milligrams once or twice a week to a total of 10 to 12 injections. These writers report relief of the pains.

In 1944 Fels made a new contribution by using large doses of testosterone propionate within a short period of time in 3 cases of cancer, 2 of which were recurrences and 1 of which was inoperable. In the first 2 patients relief of pain and other symptoms were obtained and in the third (ulcerated tumor) deodorization and reduction of pus.

In my own experience inoperable cases require a perfect follow up. In general I prescribe testosterone propionate for those patients who are being attended at home but who are not under my strict personal supervision. I can confirm that the pain diminishes to such an extent under this therapy that narcotics become unnecessary.

PROPHYLAXIS OF RECURRENCES

Because of the results obtained in many cases of mastopathy with testosterone and because I was convinced of the relationship between this disease and mammary cancer I planned in April 1939 to use testosterone as a postoperative measure in mammary cancer for the prevention of recurrences. I started using testosterone¹ in several patients with

unilateral mammary cancer and mastopathy of the other breast.

To date we have treated 63 patients with mammary cancer who had previously been operated upon. Treatment was started in 49 patients more than 1 year ago, in 12 more than 4 years, in 4 more than 5 years, and in 24 more than 3 years ago. It is believed that in view of this experience an appraisal of the results obtained to date is warranted.

As controls 64 cases are reported in which the breast had been removed by the same technique of radical surgery during the period of 1932 to 1939 and in which testosterone propionate was not used.

All 127 cases were operable and corresponded to Stages I and II of the clinical classification² which I adopted.

All but one case (No. 42229) underwent generous mastectomy with extensive removal of skin and aponeurosis, resection of the pectoralis major and minor, and dissection of the cellulolymphatic tissue of the axilla from within outward, removing all these parts in a single piece. The adipose-cellular tissue under the clavicle and as far as the supraclavicular region which is inaccessible to dissection was always coagulated electrically. In some cases a flap of the abdominal skin was used since it was impossible to make a perfect suture by simply stitching the wound.

PATHOLOGIC ANATOMY AND HISTOLOGIC GRADING OF MALIGNANCY

In all 127 cases histopathologic examinations were made.

To date no agreement regarding the classification of tumors has been reached. Great confusion exists often preventing a complete understanding between pathologists of different countries and even of different clinics. Since the classification of mammary carcinoma is no exception, the system which I have adopted should be described.

In my opinion the ideal classification from a practical point of view is one which is not

An anatomoclinical classification based on both clinical examination (including transillumination, fluoroscopy, etc.) and pathological examination. The cases are divided into 6 stages: (1) tumor localized in the mamma; (2) movable axillary metastases; (3) obstructive axillary metastases; (4) movable supraclavicular metastases; (5) obstructive supraclavicular metastases; (6) distant metastases or extensive extension of the localized lesion. This classification is of basic value for statistics and it is no doubt as to the presence or absence of axillary metastases, the degree of infiltration being confirmed by clinically.

¹Testosterone propionate used throughout usually as neo-hormonal. Other preparations are used only in some cases.

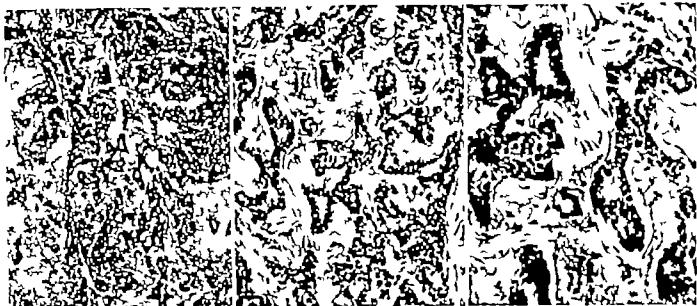


Fig. 4.

Fig. 4. Scirrhous carcinoma. The neoplastic foci form little blocks reproducing the tubular formations when observed with a central light. Objective, 8 ocular 4 bellows 5

Fig. 5

Fig. 5. Scirrhous carcinoma. The glandular appearance is

more plainly seen in this photograph. Objective, 20 ocular 4 bellows, 52.

Fig. 6

Fig. 6. Scirrhous carcinoma. A certain degree of cellular anaplasia may be seen. Objective, 40 ocular 4 bellows, 45.

crease in the dimensions of the nucleus and changes in its form and arrangement

The carcinoma adenomatosum (Figs 4-6) is a glandular malignant tumor in which however it is possible to identify the mother tissue. Although proliferation of the epi-

thelium occurs in an irregular and disorderly fashion the tumor has an inner luminosity (alveolar arrangement). The cellular restlessness is evident. There is a notable increase in the cellular dimensions with marked polymorphism. One can find monstrous nu-



Fig. 7

Fig. 7. Note the invasion of the connective tissue by solid blocks and cribs. Objective, 8 ocular 6 bellows, 35

Fig. 8

Fig. 8. The cellular anaplasia is prominent. Objective, 20 ocular 6 bellows, 35.

Fig. 9.

Fig. 9. The irregularity of the form and size of the cells, particularly of the nuclei, shows that there is a high degree of anaplasia present. Objective, 40 ocular 6 bellows, 30.

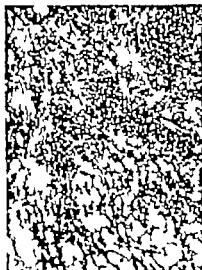


Fig.

Infiltration of the connective and fat tissue by isolated cells. Objective 8 oculi 6, bellows 35.

Fig. Not in this section light degree of cellular

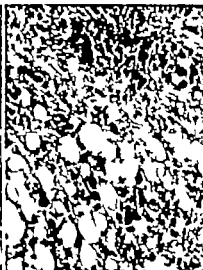


Fig.

naplasia. Objective 20, oculi 6 bellows 35.
Fig. 2. Infiltration of the muscular pectoralis major by the neoplastic cells. Objective 20 oculi 6 bellows 35.



Fig. 2.

cells emitting numerous mitoses. The tumors produce metastases after a relatively long localized stage.

The carcinoma solidum (Figs 7-9) constitutes a more common morphologic type of mammary cancer. It represents a higher degree of nondifferentiation than the tumor just discussed. The proliferous cells however do not lose the characteristics of the epithelium but form solid blocks or cords and there is no inner luminosity reminiscent of the glandular structure from which they originate. Sometimes this makes it difficult to distinguish these from certain epidermoid tumors. The atypical cytologic appearance is even more distinct and granulated structure vacuoles etc. can be found in the cells.

In the carcinoma diffusum (Figs 10-12) called meristoma by Fischer Wasels the epithelial characteristics disappear completely the contiguity of the cells forming rows or budding masses. The cells spread into the connective tissue sometimes retaining the cubic or cylindric shape but frequently keeping their round or globular appearance. The differential diagnosis from sarcoma is not always easy for which reason Fischer Wasels tried to combine these tumors with the carcinomas and sarcomas into one group the meristomas.

The above classification is made according to a system. The pure forms are rarely found. Sometimes one tumor can have the appearance of two consecutive grades. Zones of adenoma malignum and areas of carcinoma adenomatousum are often found together but on no occasion have carcinoma diffusum and adenoma malignum or carcinoma adenomatousum been found to coexist.

It is logical that when two forms coexist the grading of malignancy should be made according to which kind predominates. If both forms occur to the same degree this should be indicated by an intermediate grade. In a case of mammary tumor for instance in which carcinoma adenomatousum and carcinoma solidum occur to the same extent the grading would be II-III.

This method of grading is, of course open to criticism. One of its weak points is that the reaction of the connective tissue is not taken into consideration. I agree that a scirrhous carcinoma differs from a medullary tumor. The development of the clinical case will differ in the same way as the sensitivity to radiation.

I believe however that these considerations should be thought of as secondary since there is not the slightest doubt that the degree of differentiation of the epithelial elements reflects much more clearly the degree of malignancy.

nancy of a carcinoma than does the connective tissue reaction. The reaction of the stroma should however always be stated in the histologic reports because it constitutes to a certain degree an indication of defense against malignant proliferation.

Recently I have checked this system of grading clinically in a study of 308 cases of mammary cancer which were reported to the

Associação Paulista de Medicina. The postoperative results observed over a period of more than 5 years were for each stage of malignancy as follows: grade I adenoma malignum 100 per cent; grade II carcinoma adenomatousum 60 per cent; grade III carcinoma solidum 23.4 per cent; and grade IV carcinoma diffusum 0 per cent.

SUMMARY OF RESULTS

As mentioned 63 patients with mammary cancer (grades I and II) were treated with testosterone propionate after having undergone radical mastectomy. Of these 49 patients had been operated upon more than 1 year ago. Space limitations prohibit their detailed report. However the accompanying tables and case reports summarize the overall results obtained.

COMPLETE REPORT OF SIX CASES

CASE No. 40030. I. T. 43 years of age married came for first consultation on December 26, 1939. Clinical diagnosis: carcinoma of a left supernumerary breast. Upon physical examination the clinical stage could not be determined exactly because of the extreme obesity of the patient. The patient had always had a small pit below the left breast but paid no attention to it until he noticed it growing and forming a tumor about 3 months before. Examination revealed a hardened, aberrant left breast, the size of a hen's egg with an irregular surface. No change in the normal breast could be observed by palpation or x-ray. Lymph nodes in the corresponding axilla appeared not to be involved. The clinical examination was not conclusive because of the patient's extreme obesity. Menstruation occurred every 28 to 30 days and lasted 3 to 5 days. There had been two normal deliveries and one miscarriage.

After operation in January 30, 1940 the upper mammary breast with its tumor was extirpated. Pathologic examination revealed a diffuse macrocellular carcinoma (metastatic) with abundant cells. The tumor showed atypical nuclei, numerous mitoses and intense infiltration of the connective

tissue into the lymphatic and blood vessels. The connective periglandular tissue showed tumorous infiltrations radiating into all directions. Even the fat tissues were infiltrated by neoplastic elements, grade IV of histologic malignancy (Prof. Moacyr Amorim).

A few days after the surgical intervention a diffuse infiltration of the subcutaneous tissue near the external borderline of the left breast was noted and various lymph nodes the size of an olive were found. Because of the high degree of malignancy of the neoplasm shown by this immediate postoperative development radical mastectomy was decided upon.

At the second operation on February 20, 1940 the breast was amputated—the Halsted operation being used with transverse incision of the axilla.

Pathologic examination confirmed the diagnosis made from the earlier examination: great infiltrations of the cellular tissue and metastases in various lymph nodes were found. Treatment with 50 milligrams of testosterone propionate per week was started during hospitalization in March 1940. In May 1940 an axillary tumor near the latissimus dorsi was noticed. Roentgen ray therapy was started and the treatment with testosterone propionate was stopped upon the patient's request. In July lymph nodes in the supraclavicular fossa became palpable and hepatic metastasis developed shortly thereafter. The patient died September 16, 1940 with symptoms of cerebral metastasis. The total dose of testosterone propionate that she had received was 350 milligrams.

CASE No. 40117. I. F. 31 years of age married came for first consultation on April 5, 1940. The clinical diagnosis was carcinoma of the right breast, clinical stage II. The patient had never experienced any symptom in the breast until a month before when she noticed a hardened zone in the right breast. She treated it with hot compresses and cream without obtaining any improvement. Examination revealed a tumor of the whole right breast which was hard and turgid and increased in size but palpation revealed no fluctuation nor were there pains either spontaneous or upon pressure. At the level of the axilla numerous lymph nodes were felt. Menstruation was very scanty, lasting 1 to 2 days and irregular, often with a delay of 5 to 10 days. There had been one normal pregnancy.

Operation performed on May 11, 1940 consisted of an extensive amputation of the breast with axillary dissection and transplantation of abdominal skin in order to close the thoracic wound. Partial rupture of the sutures occurred a few days after operation. Pathologic examination revealed the neoplasm to be carcinoma diffusum with axillary lymph node involvement, grade IV of histologic malignancy. On May 30, 1940 patient was released from the hospital. Ambulatory treatment was given until July 1940 at which time the wound had healed completely. During the period 100 milligrams of testosterone propionate per week was administered. The further course of the patient was uneventful until March 1942 although the administration of



Fig. 3. Case 43. 30 P. Parallel sections of breast. I, one of the distal parts; voluminous tumor mass the size of baby's fist as found. A typical fibrous capsule surrounds the tumor separating it completely from the adjacent tissues.

testosterone propionate was irregular because of long periods of amenorrhea. On April 5, 1942, the patient was brought to the hospital as an emergency case. Roentgenographic examination revealed pathologic fracture of the fifth dorsal vertebra. Complete immobilization was impossible because of the patient's extreme obesity. Roentgen-ray castration was performed and also irradiation of the vertebral column which, however, brought about only slight relief of pains. In October, 1942, the patient developed pneumonia and died on October 27, 1942. The total dose of testosterone propionate administered was 500 milligrams.

CASE No. 4. L.C. 41 years of age, married, came for first consultation on July 9, 1941. The clinical diagnosis was cancer of the left breast, clinical stage II. The patient had developed a tumor in the left breast approximately $\frac{1}{2}$ mo. ago. She had felt no pain but the progressive growth of the tumor worried her. Upon examination a tumor the size of a nut was found at the external borderline of the left breast. Transillumination showed a dark spot with no apparent demarcations. Various enlarged lymph nodes were found in the axilla some of which seemed to be an axillary extension of the mammary gland. Menstruation occurred every 16 to 8 days and lasted 3 or 3 days. There had been three normal deliveries.

Operation on July 23, 1941, consisted of radical mastectomy. The postoperative course was normal. Pathologic examination revealed a carcinoma diffusum with axillary lymph node involvement, grade IV of histologic malignancy. Treatment with testosterone propionate, 5 milligrams per week, was started immediately. The patient was released from the hospital August 24. In April 1942 pains in the vertebral column started. Roentgenograms showed no changes at all and the patient underwent treatment for rheumatism. In June of the same year the

radiculargia became worse, and the patient also complained of cough. Roentgenographic examination revealed metastases at the level of the 11th dorsal vertebra and in the lungs. At that time the patient was suffering from amenorrhea and admitted to have interrupted the testosterone propionate treatment, since she attributed her illness to that drug. She was advised nevertheless to take 175 milligrams per week. Unfortunately she followed the advice of another physician who considered this treatment inadvisable. The patient's condition deteriorated in spite of the use of rad therapy. Dyspnea developed and the general state of health rapidly became poor. The patient died in cachexia at the end of October 1942. Total dose of testosterone propionate was presumably 200 milligrams.

CASE No. 43. 092. N.R., 43 years of age, married, came for first consultation on March 9, 1941. Clinical diagnosis: cancer of the left breast, clinical stage II. For 3 months she had noticed a tumor of the left breast. She consulted a doctor who made a biopsy from which he made the diagnosis of cancer. Upon examination a large tumor without any definite demarcations was found. It was located at the outer borderline of the breast and the skin adhered to it. An infiltration of the cellular fatty tissue along the border line of the breast was observed. The lymph nodes of the axilla were found to be enlarged, the largest being the size of a nut, although it is freely movable. The patient suffered from menorrhagia, lasting 6 to 8 days, with intervals of 25 to 30 days. There had been 6 normal pregnancies.

At operation March 19, 1941, radical mastectomy was carried out. She was released from the hospital on March 4, 1942, on which day treatment with testosterone propionate 75 milligrams per week was started. Pathologic findings: carcinoma diffusum with lymph node involvement, grade IV of histologic malignancy. Patient returned on August 7, 1941, complaining of severe pains in the vertebral column and edema of the left arm. Roentgenographic examination revealed metastases at the level of the 11th dorsal vertebra. Upon palpation of the supraclavicular fossa, a hard tumor was found which was scarcely movable and seemed to be fixed to the lymph nodes of that area. In the axilla and near the latissimus dorsi spreading to the back, an infiltration of the cellular subcutaneous tissue was observed. Roentgen-ray castration was performed and roentgen ray therapy was used for the various affected areas, but it was not possible to establish a satisfactory dose since the patient's general health was deteriorating. In October 1942 the patient began coughing and expectorated blood. At this time a new tumor was found at the level of the 5th intercostal space below the zone of operation, and dissemination

of small tumorous nodes had occurred not only into the axillary region and anterior wall of the chest, but also into other distant regions of the tegument. Patient died on January 9, 1943. The total dose of testosterone propionate could not be determined accurately but it did not exceed 200 milligrams.



Fig. 14.

Fig. 15.

Fig. 16.

Fig. 14. Same case. Comedocarcinoma of ducts, with diffuse infiltration. Low power. Marked interstitial sclerosis between cancerous cystic formations. Small sclerotic capsule formation around the smaller focus. Inside this capsule a strong lymphocytic infiltration is visible. A small focus shows small adenocarcinoma proliferation with solid cords progressing toward the tissue of the capsule.

Fig. 15. Same case, same slide slightly higher power. This field shows small areas of cancerous proliferation, around which a kind of a capsule of fibrous tissue has formed in which lumps of parvocellular elements sometimes develop (mainly lymphocytic).

Fig. 16. Same case, same slide slightly higher power. Cancerous focus or larger adenocarcinoma also surrounded by the same type of capsule vaguely outlined and showing in the central part a necrotic appearing substance with areas of visible calcification, showing black on the picture.

Adm of the normal mammary gland and thickened areas or sections of sclerosis between the adenocarcinoma foci are visible.

CASE No 42 220. MSS. 41 years of age, married (Fig. 13 to 28) came for first consultation on September 5 1939. Clinical diagnosis carcinoma of

the right breast clinical stage II. At the end of 1938 a biopsy of the right breast was made in another hospital, and on the basis of this a diagnosis of



Fig. 17.

Fig. 18.

Fig. 19.

Fig. 17. Same case, same slide slightly higher power. This field shows numerous adenocarcinoma formations with a voluminous necrotic center separated by thickened fibrous sections. Note however in the periphery corresponding to the skin of the nipple region, the formation of a genuine fibrous capsule separating the cancerous focus almost entirely from the subcutaneous tissue.

Fig. 18. Same case same field as in Figure 15 slightly higher power. Two very small foci or cancerous nests. One of these particularly is surrounded by a fibrous capsule and lymphocytic accumulations which form lymphocytic nodes.

Fig. 19. Same case same slide, moderate magnification. This field shows identical picture as in Figure 20.



Fig. 20

Fig. 20. Same case, same slide, moderate magnification. This field shows small rim of cancerization next to the acini, which still appear normal.

Fig. 20. Same case, same slide, field adjacent to that of Figure 20, showing the same phenomena. Some small, characteristically adenocarcinomatous foci are located next to small lobes with acini, which still appear normal. The other acini or tubular formations are difficult to classify (possibly cancerous).



Fig.

Fig. 21. Same case, same slide, moderate magnification. This field shows a large, well-defined structure, possibly a cyst or a large glandular unit, surrounded by a dense layer of cells.



Fig. 22

Fig. 22. Same case, same slide, moderate magnification. This field shows a large, well-defined structure, possibly a cyst or a large glandular unit, surrounded by a dense layer of cells.

glandular epithelium was made. The patient did not consent to operation and was treated with injections of the content of which was unknown to her. She specified during her first visit to this hospital that she would not be subjected to surgical intervention.

Examination revealed a hard tumor of the right breast about the size of a baby's fist, about a 3-inch demarcation fixed to the skin, particularly at the level of a scar from a previous lymph node was found in the axilla. The entire



Fig. 23

Fig. 23. Same case, same field as Figure 20, higher power. Cancerous cells in the small central focus and surrounding fibrous capsule.

Fig. 24. Same case, same field as Figure 20, higher power. The acini at top are almost normal. At bottom, as if connected with above structures, are tubular formations (th



Fig. 24

proliferations or epithelial buds of cancerous appearance.

Fig. 25. Same case, same field as in Figure 24, higher power. In the center is a small tubular formation, apparently isolated by connective tissue. There are cancerous proliferations around it, which grow and form solid knots, infiltrating the surrounding connective tissue.



Fig. 25



Fig. 26

Fig. 27

Fig. 28

Fig. 26. Same case, same slide as that of Figure 14 but different field and higher power. Cancerous proliferation surrounded by a connective tissue capsule.

Fig. 27. Same case. Atypical epithelial proliferations apparently cancerous growing in tubular formation. They seem to be pseudopapillary but do not infiltrate the sur-

rounding capsule.

Fig. 28. Same case. This figure shows the sight of the fibrous tissue against the epithelial penetration. There are two points, one at top and one at bottom where the fibrous ring is incomplete and seems to be attempting to isolate the neoplastic focus more completely.

area of the tumor appeared dark upon transillumination without definite lines of demarcation. Menstruation was of the 28 to 32 day type and lasted 3 to 4 days. No pregnancies.

Testosterone propionate .175 milligrams per week was administered. In October 1930 the patient had a menstruation of 1 day's duration followed by 2 days during which the flow was of a clear slightly pink color. Thereafter she suffered from amenorrhea. Nevertheless the same dose of testosterone propionate was continued until March 1930 at which time he had received approximately 5000 milligrams. Another examination revealed a definite local improvement—the tumor became circumscribed and detached from the skin. The axillary lymph nodes could no longer be palpated. In spite of the extremely high dose of an androgenic hormone no signs of virilization developed. At that time the dose was reduced to .5 milligram per week which was continued through 1930 during which year the patient had only one menstruation lasting only 1 day.

In February 1931 signs of virilization developed: hypertrophy of the legs, thighs, and abdomen and enlargement of the clitoris. No voice changes were noted but the patient was not questioned in order not to cause new apprehensions. The dosage of testosterone propionate was then further reduced to .10 milligram per week and this was continued until May 1932. At that time the patient was in a good condition of health and the local condition kept improving. However the size of the mammary tumor did not decrease. The patient who was worried about the symptoms of virilization and amenorrhea finally agreed to surgical intervention on condition of

not being completely disfigured. Having heard about plastic amputation she insisted upon such an operation. In spite of the serious objections which could be raised against such a procedure I decided to perform this operation in view of the favorable clinical development and the patient's attitude.

At operation on June 7, 1932 a simple amputation of the mammary gland was performed and only the aponeurosis of the pectoralis major was extirpated. Thereupon a tranplantation of the adipose tissue taken from the abdomen as well as a free graft of the nipple properly prepared was made. The area was immobilized by a special plaster arrangement. On June 27, 1932 upon removal of the plaster a perfect integration of both grafts was observed. The patient was released from the hospital on July 1, 1932.

The following is the pathologist's report on the extirpated material:

1. Specimen consists of mammary gland part of skin and aponeurosis. When cut vertically along parallel lines a voluminous tumor mass about the size of a hen's egg is seen in a central location. This area is of nodular character, the adjacent tissues being macroscopically clearly circumscribed as if surrounded by a capsule of skin and fatty tissue and separated widely from the aponeurosis. Most of these have a grayish appearance, some are brownish red. The consistency is hard and firm in some sections and very soft in others.

2. Cut parallel to the former dissection, the most smaller nodules the size of a grain of corn preform the main tumor mass. One of these smaller nodules had a cystic appearance and was filled with a liquid of chocolate color and of gelatinous consistency.

3 In the other sections the mammary gland below the nipple area and the opposite half is extremely sclerotic, hard in consistency and whitish of color yet there are no nodules of tumorous appearance.

The histologic examination revealed the following: Sections taken from various regions of the mammary gland all show the same picture characterized by extensive areas of sclerosis and hyalinization of the gland with a high degree of edema and softening of the tissue. In some sections the center of these areas there are some isolated acini or glandular lobes atrophic and lost in the density of the sclerotic zones. In these sections some ducts also surrounded by connective tissue are particularly conspicuous, which however are greatly dilated some times cystic and lined with stratified epithelium. The latter consists of small and irregular cells which sometimes resemble the basic cellular elements. When sectioned on a tangent the epithelium appears very thick almost obliterated, the light and thus revealing the structure appears fibrous. There is however no rupture of the basal layer.

Sections taken from the tumor masses show large epithelial structures generally cystic appearance, formed by glandular proliferated epithelium of typical character and filled with thick contents of a secretory hyaline appearance. These masses are surrounded by epithelial trunks or lines which infiltrate the adjacent connective tissue in various directions. Some of these assume an adenomatous appearance. At the points there are islands of epithelial atypical anaplastic cells in the dense connective tissue. The tumor resembles large areas of connective tissue which forms fibrous nodules around the epithelial growths. There are small nodules of calcification in the stroma. Nearby close to the fatty tissue it can be noted that the neoplasia is progressing under formation of dilated ducts with the atypical appearance mentioned but always wrapped in strands of fibrous tissue forming a kind of fibrous capsule around them.

Diagnosis: carcinoma of the duct of the mammary gland. High degree of atrophy and sclerosis of the mammary gland. (Observations: histarctic type of a not very pronounced anaplasia grade II of histologic malignancy (Prof. Moavary Amorim).)

After surgical intervention, treatment with testosterone propionate was started in September 1943 after the patient had menstruated 3 times. The dosage administered at that time was 30 milligrams per week. On June 9, 1944 the patient was doing well, had had no recurrences but had had amenorrhea since April. The appearance of the reconstructed breast was satisfactory. The total dose of testosterone propionate was 7,800 milligrams.

CASE No. 43,044 W. A. L. 46 years of age married came for first consultation on January 5, 1943. Clinical diagnosis: cancer of the right breast (clinical stage II). Patient had noticed for some time the level of the right breast the appearance of a small tumor to which she attached no importance. Its rapid growth, however, caused her to come to this

clinic. Examination showed a large increase of the size of the mammary gland, which was rigid and the mobility of the skin over the deep tissue had disappeared. Palpation revealed that the whole mammary gland was transformed into a hard tumor which seemed to be fixed to the deep layers. On transillumination a very dark spot which occupied the entire area, could be seen. In the axilla numerous lymph nodes, some the size of a pigeon's egg, could be palpated. Menstruation was of the 38 day type lasting 5 days. There had been five normal pregnancies.

At operation on January 28, 1943 a radical amputation of the breast was performed, followed by plastic surgery, an abdominal flap being used to make up for the extensive loss of substance of the tegument. The postoperative period was normal. The patient was released from the hospital on February 8, 1943. On February 1, 1943 treatment with 75 milligrams of testosterone propionate per week was started.

Pathologic findings: Carcinoma diffusum of lymph node involvement, grade IV of histologic malignancy. In April 1943 patient began having amenorrhea, wherefore the dosage of the hormone was reduced to 75 milligrams per week. On April 1, 1944, the patient was doing well and showed no recurrence on clinical examination. On August 29, 1944 the patient was brought to the hospital after having complained for several days of intense pain at the height of the lumbar column. On that occasion, the presence of metastases in the column was observed radiologically and lymph nodes in the supraclavicular fossa in the mid operated upon and palpated. The dosage of testosterone propionate was again increased to 75 milligrams per week. The patient is being followed up continuously.

OBSERVATIONS

The results obtained when testosterone propionate was administered after mastectomy are much better than when this postoperative treatment was omitted. One may call it a 100 per cent improvement. This figure is not absolute since the number of observed cases is still rather limited and other factors may have interfered. There is, for example, the possibility of a fortunate series of operations or that of a technical superiority of the surgery which may have to be considered. Improvement in surgical technique in this series cannot be eliminated entirely as a contributing factor. However if this were the case, one would have to assume that the technique acquired over many years of practice has been superior during this particular and limited period of time as compared with that used in the earlier cases not treated with testosterone propionate.

TABLE I—GENERAL STATISTICS

115-nine patients operated on (Clinical Stages I and II) and treated postoperatively with testosterone propionate for more than 1 year

Years since operation	Number of patients operated on	Number of patients followed up	Recurrences	Survival about recurrences Per cent
				9 90
2-3	3	3		84.6
3-4			—	00
4-5	8	6		4 66.6
More than 5		4	—	4 00
Total	49	43	8	30 85.6

Comparison of our results after testosterone propionate treatment with the data from the best clinics not using this postoperative therapy shows the superiority of our method

In my opinion there exists sufficient clinical and experimental evidence to justify the conclusion that testosterone propionate has a prophylactic effect against recurrences of mammary cancer after operations

The mechanism of this effect has not yet been explained definitely. However in view of the atrophy of the anterior pituitary in rats after testosterone administration as observed by Lacassagne (33) and others and the hypothesis of Moore and Price that the pituitary plays an intermediary rôle it seems probable that the effect of testosterone in mammary cancer is mediated through the pituitary gland

For the interpretation of the inhibitive or prophylactic effect of testosterone propionate against recurrences of mammary cancer it is necessary to consider two types of cases (1) that in which all neoplastic elements are removed and (2) that in which there are remaining neoplastic elements

TABLE II—RESULTS WITH AND WITHOUT TESTOSTERONE PROPIONATE

Patients with clinical stages I and II during a postoperative period of more than 3 years.

Testosterone propionate treatment	Period	Number of patients	Number of patients followed up	Recurrences	Survival about recurrences	
					No	Per cent
Yes	950-94	4			9	90.4
No	32-936	64	43	4	1	40

TABLE III—RESULTS WITH AND WITHOUT TESTOSTERONE PROPIONATE

Patients with and without auxiliary metastases during a postoperative period of more than 3 years.

Testosterone propionate treatment	Auxiliary metastases	Number of patients	Number of patients followed up	Recurrences	Survival without recurrences	
					No	Per cent
Yes	No	5	3	—	3	00
Yes	Yes	9	6		4	87.5
No	No	9	7	—	7	00
No	Yes	55	55	24	4	16.8

If the operation performed is entirely radical i.e. all neoplastic elements are removed a recurrence can occur only by extension of malignancy to the opposite breast where the tissue matter still exists. This would mean that the recurrence of the tumor is not brought about by remnant neoplastic cells but rather by the formation of a new tumor on the basis of pre-existing cancerogenic factors. According to observations estrogens seem to be the principal cancerogenic element with respect to the mammary gland. Therefore the biologic neutralization of the estrogenic element by testosterone would partly remove the danger of recurrence.

In cases in which neoplastic elements remain after operation one of the phenomena observed after the administration of testosterone propionate is the formation of dense fibrous tissue as mentioned by Fels and observed by me in case No. 42229 in which fibrous capsules were actually found. It is probable that this process limits or even prevents the development of further neoplastic tissue by destruction of the tumor through

TABLE IV—RESULTS WITH AND WITHOUT TESTOSTERONE PROPIONATE

Patients with clinical stages I and II during a postoperative period of more than 4 years.

Testosterone propionate treatment	Period	Number of patients	Number of patients followed up	Recurrences	Survival about recurrences	
					No	Per cent
Yes	939-940				8	80
No	92-9	64	5	5	20	44.4

TABLE V—RESULTS WITH AND WITHOUT TESTOSTERONE PROPIONATE

1 (tent th and thout villary metast d ng postoperative period of more than 4 years

Testosterone propionate treatment	Attilar metastases	Number of patients	Number of patients followed up	Recurrences	Survival without recurrences
					No. Per cent
Yes	N				00
Yes	Yes				
N	N				
No	Yes				

complete blocking. This interpretation is merely a hypothesis which must be confirmed by further observations before it can be accepted definitely.

The process of fibrosis directs attention to the difference between the reaction of the scirrhous and of the medullary tumor to testosterone propionate. Clinically no difference was observed but histologically it appears that the organism makes an effort to block the tumor by proliferation of fibrous tissue in which case testosterone propionate can only enhance this process. As to tumors rich in cells (medullary) fibrosis would constitute a beneficial factor probably for the purpose of defense as has been mentioned.

TABLE VI—RESULTS WITH AND WITHOUT TESTOSTERONE PROPIONATE DURING A POSTOPERATIVE PERIOD OF MORE THAN 3 YEARS¹

Patients classified according to their grade of histologic malignancy

Testosterone propionate treatment	Histologic malignancy	Number of patients	Number of patients followed up	Recurrences	Survival without recurrences
					No. Per cent
Yes	I				00
Yes	II				00
Yes	III				00
Yes	IV				
No	I	5			00
N	II		7		
N	III	48	36	8	30.7
No	IV	6	4	4	

¹The results observed in patients during 3 years postoperative period are not listed since there are only 4; all survived without recurrences.

TABLE VII—DOSAGE OF TESTOSTERONE PROPIONATE GIVEN AS PROPHYLAXIS AGAINST RECURRENCES AFTER MASTECTOMY

Attilar metastases	Side of body used	1st year mg.	2nd year mg.	3rd year mg.	4th year mg.	5th year mg.
absent	Grade I		—	—	—	—
absent	Grade II	30		75	75	
absent	Grade III		30	30	75	
absent	Grade IV	60	5	75	30	30
present	Grade I	30	5	5	5	
present	Grade II	75	30	30	15	
present	Grade III	60	5	75	30	15
present	Grade IV	7	60		75	30

*These 5 years have never been observed in treatment of the dosage used during the fifth year and after this time recommended.

It appears that the observations made in our 63 cases warrant the establishment of some rules for the prophylactic use of testosterone propionate after mastectomy. Large doses have to be used over a long period of time. While first reluctant to use large doses particularly in young women because of fear of virilization we are now inclined to believe that such side effects are of secondary importance in cancer and that they occur only in a comparatively small percentage of patients and with little intensity. Virilization was observed in 9 of 49 patients mastectomized more than 1 year ago; last year only 1 such patient was observed in a group of 14. It must be pointed out however that we do not draw the patient's attention to such phenomena in order to avoid nervous upsets which might be detrimental to the continuation of the treatment.

If a total of 10 patients showing signs of virilization the phenomenon was severe in 5, moderate in 3 and questionable in 2. In the cases considered as severe hypertrophy of the clitoris and hypertrichosis occurred in the moderate cases hypertrichosis only occurred. As to the questionable cases they were classified as such because the patients insisted that they had observed an increase in hair growth. No change in the timbre of the voice was ever observed. The attention might be called to the fact that virilization occurred essentially in young women only 9 were under 40 years of

age and only 1 was more than 40 years old (case No. 42229). Virilization occurred when the weekly dose was above 30 milligrams and the total dose reached 800 to 1500 milligrams of testosterone propionate.

Menstrual irregularities were almost the rule in women treated with testosterone propionate; these consisted of simple changes in the amount of the flow, its duration, and the length of the interval, and amenorrhea of shorter or longer duration.

In women past forty the onset of the menopause is hastened and frequently occurs a few months after the commencement of the treatment. The amenorrhea observed after treatment is of no importance, not even in young women as compared to the cancer. If the amenorrhea is accompanied by general and unpleasant phenomena (vomiting, dizziness, circulatory troubles), the dose must be reduced or, in serious cases, treatment must even be interrupted for some time to permit the patient's normal state of health to return. However, there are certain cases which are very malignant (diffuse carcinoma) in which the high doses must be maintained by all means.

The use of testosterone after the menopause seems absurd at first. However, one must realize that even in elderly women suffering from cystic mastopathia, estrogen is found in the breast.

As to the dosage to be used, the following points have to be considered: (1) histologic grade of malignancy, (2) clinical stage, (3) age, (4) menstrual cycle, (5) biotype. Except for the first two, the others are of secondary importance.

A proper dosage can be established approximately by starting with a minimum of 25 milligrams of testosterone propionate per week and raising it to a maximum of 175 milligrams per week. Within these limits the dose may be determined according to the development of the case and the reactions of the patient.

Patients with diffuse carcinoma (grade IV of histologic malignancy) should usually get the maximum dose of 175 milligrams per week, no matter what the age of the patient. Neither amenorrhea nor signs of virilization ob-

served in young women should prohibit the giving of high doses, since the extreme malignancy of these tumors justifies any secondary disturbances. The dose of 175 milligrams should be maintained during the first year. Thereafter it can be reduced to 100 milligrams during the second year, to 75 milligrams during the third and fourth, and to 50 milligrams from the fifth year on. Treatment for a 5 year period appears not to give a guaranteed protection for the future and it appears justifiable to advise continuing the treatment indefinitely, just as insulin is given in diabetes.

This recommendation is based on observations in Cases 40039, 40117, 41221, and 43044; the results of which were unsatisfactory as compared with 2 other Cases, 41056 and 41317 (not described in this article), in which no recurrences occurred.

In cases of carcinoma solidum, grade III of histologic malignancy, the average weekly dose should be 75 to 100 milligrams during the first year, depending on whether there are axillary metastases. The age of the patient does not seem to justify a reduction of dose. The dose of testosterone propionate can be reduced or even interrupted when signs of virilization appear or when a prolonged amenorrhea is accompanied by general unpleasant symptoms. As the years go on, the dosage can be reduced slowly, but a minimum weekly dose of 25 milligrams should be maintained.

In cases of carcinoma adenomatousum, grade II of histologic malignancy, the dosage depends on the presence of axillary metastases. If such are present, the dose should be 75 milligrams, but otherwise 50 milligrams per week during the first year. In cases without axillary metastases, the dosage can be adjusted for young women according to any secondary symptoms such as virilization and amenorrhea observed during the treatment.

In cases of adenoma malignum, grade I of histologic malignancy, there is no need for doses higher than 25 milligrams per week. If there is mastopathia of the remaining breast and persistence of mastodynia after operation, the androgen therapy often brings worthwhile results. The surgical statistics of cases with grade I carcinoma show 100 per cent favorable results without any other treatment.

at body temperature by a constant drip of warm gelatin Ringer solution. The mesentery was exteriorized into a transparent chamber according to a technique previously described (Zintel) for the rabbit and modified for the dog by Page and Abell (12). In the present study an improvement was introduced by placing the preparation and the microscope in a constant temperature box maintained at 37 degrees C. The arterial blood pressure was routinely recorded by cannulating the carotid following exteriorization of the tissue.

In the complete tourniquet experiments in which swelling of the limb during the tourniquet occlusion is negligible the microscopic observations were routinely made just prior to and after release of the tourniquet. In a few cases observations were made during the application of the tourniquet and no significant changes were detected.

In the venous tourniquet experiments an appreciable swelling of the occluded limb always developed within a few minutes after application of the tourniquet. For this reason the microscopic observations were begun previous to the tying of the tourniquets.

The venous tourniquet experiments were performed principally on the cat by use of the exteriorized mesentery. Control observations were made on the mesenteric vessels and the tourniquet cords were then tied to occlude only the venous circulation of the limbs. In every case the presence of a pulse in the femoral artery was determined by palpation. In some of the experiments the femoral veins were also exposed and occluded with a small serrefine clamp. Venous tourniquets on 1 and 4 limbs were applied for periods of 3 to 6 hours.

Hematocrits were determined by the Van Allen method on 0.5 cubic centimeter of blood withdrawn at approximately 1 hour intervals. An indication of the fluid loss into the injured limb was obtained by periodically measuring the circumference of the leg just below the line of the tourniquet application.

Observations of the blood vessels were recorded under the following headings: (1) caliber of vessels; (2) rate and extent of blood flow; (3) presence of periodic, intermittent caliber changes in terminal muscular vessels

(vasomotion); (4) response of terminal vessels to epinephrine; and (5) degree of pooling and stagnation of the blood.

Measurements were made with an ocular micrometer at a magnification of 86 diameters (oc. 20X obj. 2.3X). In the omentum the measured arteries ranged in caliber from 30 to 150 micra and the veins from 25 to 250 micra. In the mesentery vessels of larger caliber were measured up to 700 micra for the arteries and 950 micra for the veins. Capillaries and terminal arterioles were observed in both the omentum and mesentery under a magnification of 280.

The blood samples were drawn from the jugular vein throughout the syndrome whenever a change in reactivity was recorded in the mesenteric vessels under observation. The serum from these blood samples was tested for the presence of active humoral principles by the rat mesoappendix test previously described (6). For these tests normal 100 to 160 gram rats were anesthetized with 3 to 4 milligrams of sodium pentobarbital and the mesoappendix was exposed for microscopic observation. The blood pressure was recorded by an indirect method previously described (Duncan, Hyman and Chambers). The effect of the injection into the rat of 0.5 cubic centimeter of shock serum on blood pressure, rate of blood flow, vasomotion and response of the terminal arterioles to topically applied epinephrine was determined.

Samples were recorded as vasoexcitatory (hyperactive) when their injection induced an increased reactivity of the terminal arterioles to epinephrine. Many of the samples also accelerated vasomotion and raised the blood pressure 10 to 20 millimeters of mercury. Blood samples were recorded as vaso depressor (hyporeactive) when they brought about a decreased response to epinephrine. They also frequently blocked vasomotion and lowered the blood pressure. Samples were recorded as neutral when they brought about no change in the criteria studied except for a transitory speeding of blood flow due to the fluid introduced by the injection.

Vasomotion, a term previously employed, designates the periodic caliber changes which normally occur in the terminal arterioles at

TABLE I—COMPILATION OF 27 FATAL CASES OF A TOTAL OF 37 ANIMALS STUDIED (24 COMPLETE AND 13 VENOUS TOURNIQUETS) DATA ARE ARRANGED INTO THREE CATEGORIES ACCORDING TO RELATIVE PREDOMINANCE OF HYPERREACTIVE OR HYPOREACTIVE VASCULAR CHANGES

Animal	Type of tourniquet	Duration of tourniquet hours	N. of animals	Survival time* hours	Hematocrit		Vascular reactivity				Ratio of hyper/hypo duration
							Hype		Hypo		
					Control per cent	Fatal per cent	Time* of ppear hours	Duration hours	Time* of ppear hours	Duration hours	
A. Vascular hyperreactivity predominates											
Dog	Venous, 4 legs	4		3.5	36	5	3	7	—	—	—
Dog	Complete, legs	4 to 5.5		4	33	48	3.5	3	—	—	—
Cat	Venous, legs	4.5		4	30	50	1.55	0	1.27	3	8
Dog	Complete, legs	6 to 7		3	44	61	1.5		1.5	4	4.8
B. Vascular hyperreactivity and hyporeactivity both prominent											
Cat	Venous, legs	5.0		7.8	30	40	1.3	3	1.55	5	
Cat	Venous, leg	6		5.5	33	30	1.6		1.45		8
Dog	Complete, legs	6 to 7	5	5 to 6	48	55	at 5		1.5	8	3
Cat	Complete, leg	5		4.5	34	4	1.45	5	1.5		3
Dog	Complete, legs (taped)	6 to 7		7	45	54	1.6	7.5	1.3	7.5	8
C. Vascular hyporeactivity predominates											
Cat	Venous, leg	6		8	34	4	at 6	5	at 3		5
Dog	Complete, legs (taped)	6 to 7		4.5 to 5	4	43	1.6	5	1.3		6
Dog	Complete, legs	6 to 7		3 to 4	44	40	1.6		1.5	5	5
Dog	Complete, legs	10		5 to 3	40	43	1.7	5	1		10 to 8
Rabbit	Complete, leg	6.5		4.5	38	4	at 3	8	1	3	9
Cat	Complete, leg	6		3.5	40	7	at 5	1	1	5	10

*Time in complete tourniquet experiments, refers to time after release of tourniquets and, in venous experiments, 1 time after tying of cords.

varying intervals and which are of importance in regulating the distribution of blood to the capillary bed. During the shock syndrome the vasomotion generally becomes augmented and then depressed. By augmented is meant a condition in which the frequency of periodic contraction relaxation cycles is increased and in which the constrictor phase becomes increasingly predominant (for details see Chambers and Zweifach 4). By decreased is meant a condition in which the frequency of the contraction relaxation cycle is diminished below normal and in which the dilator phase becomes progressively predominant. A stage is finally reached in which the vasomotion ceases with the terminal arterioles remaining in the relaxed state.

The reaction of the terminal arterioles to the topical application of varying concentrations of epinephrine was determined according to a technique previously described (Chambers and

Zweifach 4). The minimal effective concentration of epinephrine was that which produced a temporary contraction of the terminal arterioles so as to slow or interrupt the capillary flow for 10 to 20 seconds. This concentration was recorded as the minimal effective concentration for a given case.

Autopsies were routinely made on the viscera and the limbs.

EXPERIMENTAL OBSERVATIONS

A total of 37 animals—dogs, cats, and rabbits (see Table I)—were studied. Of these 24 developed fatal shock. The data are presented on the basis of the circulatory changes observed rather than of a statistical analysis of each type of tourniquet procedure. About 95 rats were used for the mesoappendix tests of blood samples.

General survey of circulatory changes. A study of the normal capillary circulation in the omentum

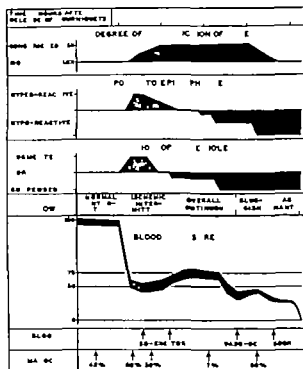


Chart. Protocol illustrating vascular changes typical of intermediate category in which both hyperreactivity and hyporeactivity are prominent. Dog No. 7, male, weight 8.5 kilograms, sodium pentobarbital, 30 milligrams per kilogram body weight, subjected to complete tourniquet of hind limbs for 6 to 7 hours. Degree of constriction and "Response to epinephrine" are expressed as multiples or fractions of the normal. Deviations are charted above or below the normal base line. Vasomotion (Intermittent arteriolar caliber changes) is expressed as the proportion of time that constrictor phase persists in relation to relaxation phase. When "augmented" the constrictor phase predominates and vice versa when diminished. When "suspended" the relaxation phase persists.

tum and mesentery has made possible the selection of several well defined vascular reactions which have been found to be affected consistently in traumatic shock (5-18). The reactions are specific enough to distinguish the circulatory effects of fluid loss *per se* from those of other conditions in the shock syndrome.

The stages in tourniquet shock which lead to circulatory collapse can be resolved into two all inclusive categories. This was always found to be the case regardless of the variations in the experimental procedure or of complications introduced by the individual variations in the natural resistance of the experimental animals.

The two categories have been designated as hyperreactive and hyporeactive. One is con-

cerned with compensatory vasoconstrictor actions to fluid loss and the other with compensatory reactions associated with the deterioration of the physiological responses of the terminal blood vessels. The interplay of the two groups of reactions, as to extent, duration and suspension of one or the other appears to account for all the variations observed.

The animals were classified under three general patterns of vascular response on the basis of the relative duration and intensity of hyperreactivity and hyporeactivity. This is indicated in Table I under A, B and C.

In one set of animals A, the hyperreactive pattern was emphasized. It developed early and persisted during the greater part of the syndrome hyporeactivity appearing only during the terminal minutes or not at all. The hyperreactive circulation was characterized by vasoconstriction, capillary ischemia, augmented vasomotion and heightened responsiveness to epinephrine. Death occurred with marked peripheral ischemia.

In the second set of animals C, the hyporeactive pattern was emphasized. It appeared early, was of long duration and was preceded by a brief hyperreactive state or almost by none. The hyporeactive circulation was characterized by a progressive slowing and eventual suspension of vasomotion, filling of the capillaries and of the collecting venules with increasing amounts of blood, a subnormal responsiveness to epinephrine and finally a partial relaxation first of the terminal arterioles and later of the arteries and veins. Death occurred with considerable congestion of the capillaries and venules.

In the third set of animals B intermediate between the above extremes, hyperreactivity and hyporeactive patterns were equally prominent. There was considerable variability in the extent to which hyporeactivity progressed in each animal apparently depending in large part upon the degree to which the blood flow had already been curtailed by the initial hyperreactivity.

Description of the circulatory responses. Complete tourniquet occlusion of the circulation in two hind limbs was carried out for periods of 4 to 15 hours on dogs under pentobarbital anesthesia (Table I). The largest number of ex-

TABLE II.—CHANGES IN CALIBER OF LARGE BLOOD VESSELS IN OMENTUM AND MESENTERY DURING FATAL TOURNIQUET SHOCK

Time* per cent	Hyperreactive category				Intermediate category				Hyporeactive category			
	A ₁	V	A ₂	V	A ₁	V	A ₂	V	A	V	A ₂	V
	90	35	4	20	8	07	07	75	5		43	64
5	66	20		24	5	87	5	7			43	64
10	66	05	5	8	45		60	78	5	5	40	66
20	54	03	0		60	05	60	78	5	30	43	60
30	43	00	0		73	5	64	8	5	30	47	7
40	60	5	8	4	8	08	67	90	5	10	47	73
50	7	7		4	8	5	68	02	5	35	48	75
60	60	04	6	20	73		60	84	05		70	67

A₁, arteries; A₂, arterioles; V and V₂, their corresponding veins and venules. Diameters of vessels are in microns, the figures being taken from typical experiments in each category.

*Time is indicated as percentage of total posttourniquet period. Terminal vasoconstriction, during agonal death period, is indicated at 00 per cent.

periments were with 6 to 7 hour tourniquets in which fatal shock occurred in a high percentage of the cases.

Out of a total of 8 dogs in the group in which complete tourniquet occlusion of 2 hind limbs for 6 to 7 hours was carried out 1 dog showed hyperreactivity which persisted through the greater part of the syndrome 2 dogs showed a comparatively short period of hyperreactivity followed by a pronounced hyporeactive stage and 5 showed an intermediate condition in which the periods of hyperreactivity and hyporeactivity were more nearly equal. The intermediate constituted the largest group and is discussed first.

The vascular reactions characteristic of the animals in the intermediate category are shown in Chart 1 which is a diagrammatic presentation of the protocol data of a typical member. The initial change following release of the tourniquets was an abrupt lowering of blood pressure which occurred within 1 to 3 minutes after release of the tourniquet before any significant swelling of the leg could be detected. There was no marked change in the caliber of the omental blood vessels and only a moderate slowing of the flow in the peripheral vessels.

Within 10 to 15 minutes the swelling of the legs became appreciable and reached a maximum within 1 to 2 hours the circumference of the limbs increasing by 16 to 19 per cent over the control. During this period of swelling the larger vessels in the omentum especially the arteries and larger arterioles nar-

rowed to about half of their original caliber (Table II). At about the same time the intermittent caliber changes of the terminal arterioles became more frequent and maintained the constricted state for a relatively longer proportion of the total period. This was especially pronounced in the precapillary junctions sphincter like arrangements of muscle about the proximal end of the side branches leading from the terminal arterioles into the capillaries. During this period of ischemia a continuous circulation coursed only through the most direct channels from artery to vein. The hyperreactivity of the terminal blood vessels at this stage was further indicated by their response to dilutions of epinephrine averaging one part in 10 to 12 million as compared with control values of one part in 3 to 4 million.

Blood samples taken during the hyperreactive period were found to be markedly vasoconstrictor when tested on the terminal blood vessels in the mesoappendix of normal rats. They produced on intravenous injection in the test animals three or four times the epinephrine reactivity a transient ischemia of the capillary bed and in some instances a blood pressure rise of 15 to 20 millimeters of mercury. The hyperreactive effects on the rat circulation persisted for 20 to 35 minutes.

During the ensuing 1 to 2 hours in the shocked dog there appeared a progressive slowing of the blood flow through the omental vessels especially in the venules draining the capillary bed and in the small veins.

nant for some time. The constriction persisted until death and was present at autopsy. Thus the consistent finds of vasoconstriction at autopsy bear no relation to the progressive changes observed during the stages leading to collapse.

At autopsy the liver and gastrointestinal tract were moderately congested. The serosal surface of the gut was purplish. The mucosa was congested throughout and the duodenal portion was frequently hemorrhagic. The cut surface of the kidney appeared ischemic. The adrenals were markedly congested especially in the medulla.

In the 1 dog which came under the *hyperactive* category the hind limbs showed a greater degree of swelling than did those in other members of the 6 to 7 hour tourniquet series the increase in circumference being about 24 to 25 per cent above the control. Vasoconstriction of the arterial vessels was marked (Table II) and was accompanied by wide spread ischemia. Within 10 minutes after release of the tourniquets vasomotion of the terminal arterioles in the omentum became more rapid with the contraction phase of the cycle persisting 4 to 5 times longer than the relaxation phase. This augmented condition lasted for about 3 hours and at the peak the terminal arterioles responded to one part in 16 million of epinephrine as compared with the initial control response to one part in 4 million. However in contrast to the conditions in the intermediate group the blood flow through the bed was markedly curtailed by the extreme vasoconstriction and hyperactivity. This condition persisted for slightly more than 2 hours when an abrupt transition into a hyporeactive state became apparent.

The differences between the hyperactive and intermediate categories are strikingly brought out in Chart 2 in which the three categories of vascular response are compared with one another. About 10 minutes before death vasomotion became less pronounced epinephrine reactivity fell sharply to subnormal levels and arterial relaxation occurred. The epinephrine reactivity although continuously falling from its hyperactive peak never became hyporeactive to the extent of complete

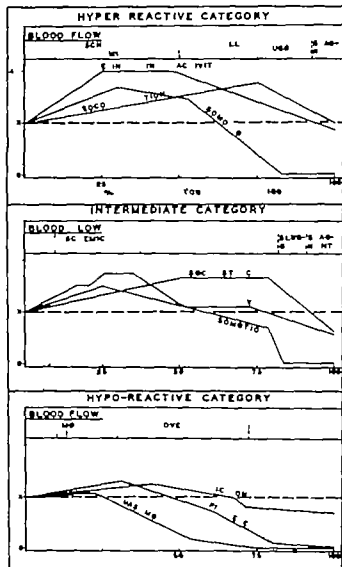


Chart 2. Comparison of significant changes in vascular reactions during fatal tourniquet experiments. Data represent averages compiled from 27 animals, 8 in hyperactive, 10 in intermediate and 9 in hyporeactive category. Normal value is expressed as 1X; the changes during syndrome as multiples or fractions of normal value.

unresponsiveness to epinephrine. A constrictor response to 1 part in 2 million (control value being 1 part in 4 million) was obtained at 15 minutes before death. There was some pooling of blood and stagnation in the venules and in the capillaries leading into them.

At the time of circulatory collapse the capillary bed was still ischemic when compared with the control but contained more blood than had been present during the early hyperactive stage.

In the hyporeactive category were 2 dogs which underwent collapse with only moderate vasoconstriction and a considerable pooling of

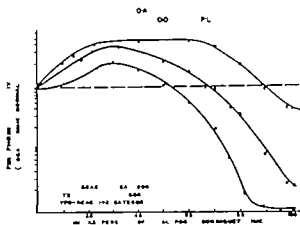


Chart 3. Reactivity of shock blood samples taken at different times during the syndrome in fatal tourniquet experiments. The three categories, hyperreactive C intermediate B and hyporeactive L, are charted separately using logarithmic scale to plot the concentration of epinephrine to which standard vasoconstrictor response is obtained. Control epinephrine value is expressed as 0 (broken horizontal line). Changes from normal are expressed as multiples or fractions of control value above base line, vasoconstrictor below base line, vasodepressor. The data are based on rat mesoappendix tests of 95 separate samples obtained at intervals during the shock syndrome. On the average 3 to 4 samples were used from each of 7 fatal experiments.

blood in the capillary bed (Table I). The injured limbs swelled only slightly after release of the tourniquets; the circumference increasing about 10 per cent over that of the control value. The initial fall in blood pressure was as great as in the preceding experiments but the pressure never leveled off and continued to fall throughout.

Vasoconstriction did not appear until about 30 to 40 minutes after release of the tourniquets. It was only moderate in character, the narrowing being about 12 to 16 per cent in the arteries and arterioles as compared with the 50 to 60 per cent usually observed in other 2 limb tourniquet experiments. Vasomotion gradually disappeared without ever having become more rapid than normal. The response to epinephrine rose slightly from the control level of about 1 part in 3 million to 1 part in 5 million and remained slightly hyperreactive for only 15 to 20 minutes. Peripheral circulation never became ischemic. An active flow persisted in all the capillaries during the first hour then progressively slowed until it became almost stagnant as early as about 2 hours after release of the tourniquets. At this

time no vasomotion was present; the terminal arterioles were completely unresponsive to epinephrine and were actually dilated. During this latter period the arteries relaxed to their control diameters followed by a slight dilatation of some of the larger arterioles (Table II). The venules contained only stagnant blood and in some areas a backflow into the capillary bed was present. Many of the capillaries also contained considerable amounts of stagnant blood. About 15 minutes before death, the flow in the arteries had become pulsatile and no forward movement existed in the capillary bed.

The hematocrit showed only a moderate increase of about 18 to 20 per cent above the control in these 2 dogs.

Blood samples were vasoexcitator only during the first 25 to 35 minutes following the release of the tourniquets and became increasingly vasodepressor from then on. A blood sample from one of the dogs taken 20 minutes before death produced in the test rat a hyporeactive response which persisted for over an hour.

The changes in the three categories may be analyzed as follows. The vascular changes occurred in the same relative sequence despite the variability of the relative lengths of the hyporeactive and hyperreactive periods. Reactions of the larger and smaller blood vessels were always in the same general direction. During the hyperreactive stage vasoconstriction of the larger blood vessels was accompanied in the terminal blood vessels by its counterpart, an augmented vasomotion and an increased responsiveness to epinephrine. Hyporeactivity appeared first in the terminal blood vessels and subsequently the larger blood vessels showed a similar tendency by their relaxation (Chart 2). In these cases, the disappearance of vasomotion and fall in epinephrine response from its hyperreactive peak occurred while the vasoconstriction of the larger blood vessels still persisted. In the 2 dogs which developed a markedly hyporeactive condition early, the tendency toward relaxation appeared simultaneously in both the larger and terminal blood vessels.

The development of humoral vasoconstrictor and vasodepressors closely parallels the vascular changes in the 3 categories of animals.

The gradual appearance of hyporeactivity in the intermediate category in contrast to the abrupt transition between hyperreactivity and hyporeactivity which occurred early in the extreme hyporeactive category is well demonstrated in Chart 3.

In conclusion it may be stated that in some experiments hyporeactivity was preceded by vasoconstriction and hemoconcentration. In others hyporeactivity was preceded by vasoconstriction alone and not by any significant change in hemoconcentration. In still others and this point should be emphasized hyporeactivity progressively developed without a significant preceding vasoconstriction or hemoconcentration.

In the group in which tourniquets were applied to *2 hind limbs for less than 6 hours* 1 dog with a 4 hour tourniquet application survived for more than 8 hours after the release of the tourniquet at which time it was sacrificed. Two dogs to which tourniquets were applied 5 and 5.5 hours died in 6 and 7 hours respectively after release of the tourniquet. The circulatory collapse in these 2 fatal cases was of the hyperreactive type in which hyperreactivity persisted for 4 to 5 hours and was followed only during the final hour of the syndrome by a gradual deterioration of the peripheral circulation.

The blood samples were hyperreactive during the first 2 hours following release of the tourniquets and then for almost 3 hours remained neutral i.e. gave no test response. This long neutral or transitional period persisted until about 30 minutes before collapse ensued, a hyporeactive blood sample being obtained in 1 case 30 minutes and in the other 25 minutes before death.

Thus the shorter duration of tourniquet occlusion favored a hyperreactive type of circulatory collapse. Under these conditions, vasoconstriction was a prominent feature during the phases leading to collapse.

In the group in which tourniquets were applied to *2 hind limbs for more than 7 hours* 4 experiments were made. In 2 dogs for 10 to 12 hours and in 2 for 15 hours. Both dogs in the 10 to 12 hour tourniquet group died whereas the 2 dogs in the 15 hour group survived and were sacrificed.

The essential difference between the 2 sets of experiments was the failure of the circulation to return to the limbs which had been occluded for 15 hours. They remained cold the toe pads did not bleed when incised and the limbs showed no appreciable swelling. No vasoconstriction was observed in the visceral blood vessels and no change either in vasomotion or epinephrine reactivity was detected. The blood flow through the peripheral vessels remained relatively unchanged for a period of 6 to 7 hours at which time the animals were sacrificed.

The lethal 10 to 12 hour experiments showed the most marked development of a hyporeactive condition of all the two limb tourniquet experiments. The initial blood pressure drop was not as marked as in all previous experiments falling from a control value in 1 instance of 140 to 80 millimeters of mercury and in the other of 150 to 84 millimeters of mercury. Circulatory collapse was obtained in both instances with almost no initial vasoconstriction and with only a very slight increase in hematocrit. Constriction of the larger blood vessels was negligible and in all instances relaxation occurred within 1 hour after release of the tourniquets. The veins became slightly dilated about the same time that the arteries began to relax. The circulation deteriorated rapidly and showed marked congestion and stagnation in the venules and in the inflowing capillaries.

The blood samples were vasodepressor in 1 instance 70 minutes and in the other 95 minutes after release of the tourniquets. Hyporeactivity was detected earlier than in any of the other experiments in the present study.

Thus provided circulation was restored to the damaged limbs the hyporeactivity became increasingly evident when the period of tourniquet application was in excess of 7 hours.

In a group of 7 dogs *both hind limbs were taped* before tourniquets were tied for a period of 6 to 7 hours. The tape was applied just tightly enough to diminish the swelling which occurs after release of the tourniquets. Only 4 of the 7 dogs died in contrast to the 6 to 7 hour experiments in which limbs were not taped and all the dogs died. None of the dogs in the series in which the limbs were taped

died with a hyperreactive pattern of vascular response.

The initial fall in blood pressure immediately on release of the tourniquets was very similar to that obtained in experiments in which limbs were not taped. The blood pressure usually fell to the 50 to 70 millimeters of mercury range irrespective of the ultimate fate of the animal.

In 2 dogs the taping was loose enough to permit some swelling of the leg and fatal circulatory collapse occurred within 5 hours after release of the tourniquets. Both dogs showed the usual sequence of initial hyperreactive change followed by hyporeactive changes in the omentum and mesentery. In 1 dog the vasoconstriction of the larger vessels was as marked as in the untaped animal and there was a considerable rise in hematocrit from 45 per cent to 60 per cent. In the other dog only a moderate vasoconstriction occurred and the peripheral blood flow remained good for almost 3 1/2 hours before hyporeactivity ensued.

In 5 of the 7 taping experiments there was no significant swelling of the damaged limbs. Three of these 5 animals survived and showed no appreciable vasoconstriction, almost no change in hematocrit and only a moderate slowing of blood flow in the mesentery and omentum. They had a blood pressure of 55 to 65 millimeters throughout the 8 to 10 hours of observation and were then sacrificed.

Two of the 5 dogs died despite the almost complete absence of swelling in the damaged limbs. In these vasoconstriction was practically negligible, a transient narrowing in caliber appearing only in some of the 50 to 60 micra arterioles. The hematocrit level remained remarkably constant during the period in which the peripheral circulation was deteriorating and then rose slightly during the final 1 to 1 1/2 hours of the syndrome. There was no restriction in capillary circulation of the type following augmented vasomotion as previously described. Vasomotion was abolished within 1 hour after the release of the tourniquets. The epinephrine response increased to a twofold maximum but did not maintain this peak and fell progressively to subnormal levels. The slowing in blood flow became increasingly evident on the venous side of the peripheral cir-

culation and was followed by a pronounced pooling of blood in the collecting venules and small veins. Death occurred with considerable congestion and stasis in the capillaries.

Blood samples produced essentially the same sequence of reactions as were found in similar untaping experiments.

In general, the taping was found to permit the maintenance of an adequate visceral circulation for longer periods of time than in untaped animals. This is probably related to the fact that less fluid was lost into the tape limb. All of the dogs whose limbs were taped and tourniquets applied showed at autopsy a considerable congestion and hyperemia of the viscera. The gastrointestinal tract, liver and kidney were especially congested. The mucosal surface of the gut was hemorrhagic, especially in the duodenal region. The kidney appeared distended and on being incised bled freely in contrast to the ischemic condition usually found in untaped experiments.

In the experiments with *complete tourniquet occlusion of 1 limb* it was found that fat shock in dogs could not be induced in periods of 8 to 10 1/2 hours by this means. The circulatory data for fatal one limb tourniquets were obtained in 3 cats and 1 rabbit which went into fatal shock with 6 to 7 hour 1 limb tourniquets. The microscopic observations were made with the transparent mesenteric chamber technique. The animals died from 2 to 4 1/2 hours after release of the tourniquets and showed a sequence of vascular changes which was predominantly hyporeactive. Vasoconstriction was moderate and in 2 cases did not appear at all. Circulatory collapse occurred with considerable congestion and stasis through the peripheral vessels.

The vascular reactions following the application of *venous tourniquets* were observed in the mesentery of cats and omentum of dogs. Circulatory changes appeared within a relatively short time after the tying of the cords, whereas with complete tourniquets no significant changes in the peripheral vessels were observed prior to the release of the tourniquets. With complete tourniquets, the few instances in which there occurred an increase in hematocrit and slowing of blood flow prior to release of the tourniquet were probably at

tributable to the unsatisfactory application of the tourniquets. In the dog it was more difficult than in the cat or rabbit to tie a tourniquet which was unquestionably complete without producing considerable trauma under the rubber tourniquets. This difference appeared to be related to the toughness in the dog of the leg musculature in contrast to the soft flabby muscles of the cat and rabbit.

Venous tourniquets on 4 legs for 3 5 hours and on 2 limbs for 4 hours produced fatal shock characterized by an exaggerated hyperreactive pattern of response. Vasoconstriction appeared within 10 minutes after the cords had been applied and increased progressively until at the end of 1 5 to 2 hours the larger arteries were constricted to one third their original diameters. During the first half of this period the blood pressure was actually 30 to 40 millimeters of mercury higher than the control levels. The capillary circulation was markedly ischemic with a continuous flow only through a few vessels. Vasoconstriction of the terminal arterioles was pronounced and the constrictor phase was so intense as to interrupt the flow for as long as 2 to 3 minutes. The blood pressure then began to fall and over a period of an hour had shown a drop of over 100 millimeters of mercury. During this period the flow in the venules and small veins became considerably slowed and finally intermittent. Of the 3 animals (Table I) which died with this type of vascular change 1 maintained the constricted condition until about 20 minutes before the tourniquets were untied upon which relaxation of the constricted condition occurred. In the 2 other animals 1 underwent relaxation about 10 minutes after the tourniquets were released and 1 died within 35 minutes after release of the tourniquets with no relaxation. Death occurred in all 3 animals with an ischemic peripheral circulation. Blood samples were vasoexcitator throughout the syndrome.

Venous occlusion of 2 limbs for 5 hours (2 cats) and 1 limb for 6 hours (3 cats) produced fatal shock in 4 of the 5 cases. The circulatory response showed a hyperreactive state during the initial 3 to 4 hours in which the tourniquets were left in place which was followed by a subsequent hyporeactive pat-

tern. In the 2 animals subjected to fatal 1 limb 6 hour tourniquets the vascular response showed a pronounced hyporeactive condition in the final hour of the syndrome. Blood samples were moderately vasodepressor only during the final 40 to 45 minutes prior to death.

EVALUATION OF STUDY

The establishment of definitive criteria by microscopic observations of the vessels directly concerned with circulatory collapse permitted a critical analysis of the factors underlying the shock syndrome. The tourniquet shock syndrome could be resolved into two sets of reactions: *compensatory and decompensatory*, which could be distinguished by specific vascular changes in the omentum and mesentery involving on the one hand the intensity of vasoconstrictor changes and, on the other, the interaction of hyperreactivity as against hyporeactivity in the peripheral circulation. Both the compensatory and the decompensatory changes contributed to the development of the markedly reduced blood flow characteristic of fatal shock. The former induced a reduction in blood flow through a widespread vasoconstriction and hyperreactivity of the terminal blood vessels while the latter impaired the peripheral circulation through interference with the intermittent constriction of the terminal arterioles and precapillary sphincters which regulate the extent and distribution of blood flow in the capillary bed.

It is generally agreed that the circulatory failure characteristic of traumatic shock is essentially initiated by a reduced blood volume (Blalock, Wiggers, Kety and Pope). Most of the recent work has stressed fluid loss into the traumatized tissue as the primary factor responsible for the fatal reduction in blood volume. The present study on tourniquet shock lays emphasis on the decompensatory changes in the terminal vessels as playing an important rôle in reducing the circulating blood volume to critical shock levels.

In the omentum and mesentery the onset of decompensation is marked by a progressive diminution of the intermittent constriction and a relaxation of the terminal arterioles and precapillaries until spontaneous caliber changes are no longer detectable. The primary effect

is to permit active circulation through a larger number of capillaries than hitherto. At about the same time the responsiveness to epinephrine begins to fall from its hypernormal peak and ultimately reaches subnormal levels. During this period the muscular venules become completely relaxed. The net effect is a progressive slowing of the peripheral blood flow especially on the venous side. Later through relaxation also of the larger vessels there develops a further discrepancy between the available blood volume and the capacity of the vascular bed. The resultant further slowing of flow occasions pooling and stagnation in the capillary bed especially in the collecting venules—factors which serve to reduce the circulating blood volume still further and eventually lead to circulatory collapse.

Similar pooling and stagnation of blood in the peripheral circulation during hemorrhagic shock have been recently reported on the basis of direct visual observation (Zwelfach, Lee Hyman and Chambers 18; Abell and Page 13) and indirectly through studies on the distribution of tagged radioactive isotopes (Fine Seligman and Frank).

Compensatory vascular reactions were found to be related to the degree of fluid loss and decompensatory reactions to the development of so called toxic factors. Previous experiments with hemorrhage (19) have indicated that the augmentation of peripheral vascular reactivity (hyperreactive state) was related to the extravascular loss of fluid. In the present tourniquet experiments the same type of hyperreactivity appeared during the period in which the damaged limbs were swelling being most pronounced in animals showing the greatest degree of swelling. Hyperreactivity was likewise magnified when the number of limbs subjected to tourniquet occlusion was increased presumably as a result of the greater amount of fluid loss because of the larger mass of tissue involved. By contrast hyperactivity was least prominent when the swelling of the limbs was negligible. The direct relationship between fluid loss and hyperreactivity was strikingly brought out in taping experiments, where curtailment of fluid accumulation in the damaged limbs resulted in the almost complete suppression of hyperreactivity.

In the untaped animals in which both hyperreactivity and hyporeactivity developed, the hyperreactive vascular changes attending fluid loss always appeared as observed in the omentum and mesentery during the early part of the syndrome. The subsequent appearance of decompensatory or hyporeactive vascular reactions could not be ascribed to fluid loss *per se*.

Previous experiments on hemorrhagic shock (16, 17) have shown the marked influence of the anesthetic agent in favoring the development of hyporeactive vascular changes. Pentobarbital sodium was among the anesthetic agents which in the presence of a curtailed peripheral circulation, was found to predispose the animal to the elaboration of vaso-depressors. In the present experiments no attempt was made to vary this factor pentobarbital being the anesthetic agent used throughout. Care was taken that the amount of anesthetic was minimal, none being administered after the omentum or mesentery was exteriorized.

With uncomplicated hemorrhage of animals anesthetized with pentobarbital (19) hyperreactive vascular responses were obtained to within a few minutes of death. Hyporeactivity was not produced by hemorrhage procedures unless the animal was maintained artificially for a prolonged period with a severely curtailed peripheral blood flow by repeated small infusions. In tourniquet shock, no similar reduction in blood flow as observed in the omentum and mesentery preceded the development of hyporeactivity and the shift toward decompensation appeared while the peripheral blood flow was still good. It appears, therefore, that the hyporeactivity in tourniquet experiments must be related to processes occurring remote from the omentum or mesentery presumably in the traumatized limbs. Strong support for such a toxic factor is the demonstration of a vaso-depressor humoral principle in blood from shocked animals withdrawn at the time that the omentum and mesentery show hyporeactive vascular changes. The occurrence of two oppositely acting humoral principles each corresponding to the circulatory condition at the time of withdrawal is significant. Thus a vasoexcitator principle

could be detected in the blood during the period in which the reactions attending fluid loss predominate while a vasodepressor principle could be detected at the time when the visceral vessels become hyporeactive. The terms vasoexcitor and vasodepressor refer to the over all accelerating or inhibiting effect on the reactivity of the terminal blood vessels and do not refer to grosser phenomena such as blood pressure or arterial dilatation. The fact that both the larger and small blood vessels ultimately exhibit the same type of response although at different times seems to indicate that the hyperreactive and hyporeactive principles affect both sets of vessels.

Adherents to the fluid loss hypothesis point out that during shock changes appear in almost all the metabolic constituents of the blood and they have claimed that it is difficult to relate the ensuing circulatory collapse to any of these factors. However it should be emphasized that in our experiments the intravenous administration of relatively small amounts of serum from the shocked animal always reproduced in test rats precise vascular reactions characteristic of the circulation in the shock host. The fivefold to tenfold dilution of the test sample in the blood stream of the recipient makes it highly improbable that the specific vascular changes considered in the present study could be accounted for by general changes in blood or tissue metabolites referable to stagnant anoxia. The appearance of a humoral hyporeactive principle consistently at the time when the vascular reactions become hyporeactive points to its being related to a particular rather than to a broad type of metabolic change. Petechial hemorrhages are not produced by the hyporeactive principle either in the shocked animals or in animals receiving injections of shock serum. This appears to discount the contention of certain investigators (11) that the hyporeactivity is attributable to the development of bacterial toxins.

Direct observations of peripheral blood vessels during different types of experimentally induced shock have been made recently in a number of different tissues of the rat, rabbit (17) and dog (10, 18). Although all agree that a marked reduction in peripheral blood

flow is the outstanding characteristic of shock, the placing of emphasis on the reaction of the larger blood vessels (12) has stressed a vasoconstrictor tendency while emphasis on the smaller vessels (18) has stressed a dilator tendency. The present study demonstrates that both sets of reactions contribute to the circulatory collapse and that only in extreme cases does one or the other predominate. The experiments of Page and Abell (12) stressing vasoconstriction represent only one aspect of the syndrome. They have reported an intense vasoconstriction and ischemia in the mesentery of animals subjected to burns or venous tourniquets. It is to be noted that in all their experiments the trauma was applied to all 4 limbs a condition which in the present study was found to accentuate the effects of fluid loss. In the experiments now reported fatal results were obtained by a variety of venous tourniquet procedures in which there occurred a wide range of combinations of hypervascular and hypovascular reactions similar to those with complete tourniquets.

Page (11) obtained evidence for a humoral vasoconstrictor by perfusion of blood samples from animals in shock through isolated rabbit ear preparations and suggests that the subsequent relaxation of the larger blood vessels may be attributed to tachyphylaxis to vasoconstrictors. This theory does not take into account the fact that the development of a hyporeactive condition appears to be dependent upon the presence of a markedly reduced peripheral blood flow rather than upon long continued vasoconstriction. In hemorrhage hyporeactivity appeared only in those cases in which peripheral blood flow was drastically reduced irrespective of whether vasoconstriction was of long or of short duration. In tourniquet shock hyporeactivity frequently develops despite the almost complete absence of vasoconstriction and of vasoexcitor substances in the blood. A significant finding not explained by tachyphylaxis is the consistent appearance in considerable amount of a humoral hyporeactive or vasodepressor principle demonstrated in test rats as the visceral circulation of the shocked animal becomes hyporeactive.

The taping experiments throw light on the extent to which hyporeactivity in tourniquet

shock can be independent of fluid loss. Taping effectively reduces the peripheral vasoconstriction and hyperreactivity ascribable to fluid loss into the damaged limbs. Despite the curtailment of fluid loss, death occurred with hyporeactive vascular changes. Although it was almost impossible to eliminate fluid loss completely, taping demonstrated that hyporeactivity could develop in certain cases virtually independent of fluid loss.

Perhaps the most important outcome of the present study is the demonstration that a wide range of variability is an integral feature of the shock syndrome.

A broad over all picture becomes apparent when the syndrome is analyzed on the basis of relative intensity of compensatory as against decompensatory reactions. Both types of reactions were present to some degree in all our animals. Even with a fixed experimental procedure the relative rôles played by these reactions varied from animal to animal and in some cases even went to the extreme where one or the other factor became almost unappreciable.

Some of the animals went into fatal circulatory collapse with compensatory reactions, such as vasoconstriction, increased frequency of intermittent caliber changes of terminal arterioles and hyperresponsiveness to epinephrine persisting until shortly before death. In these cases the compensatory mechanisms remained intact but the resulting ischemia progressed to a point where peripheral blood flow was severely curtailed. In other animals compensatory vasoconstriction and hyperreactivity were pronounced but not sufficient to disrupt peripheral blood flow. Hyporeactivity of the terminal vessels and suspension of vasoconstriction developed only after a prolonged period of hypotension usually appearing about an hour before death. In these cases hyporeactivity appeared to be related to changes resulting from a prolonged period of poor circulation through the traumatized limbs. The presence of a reduced blood flow through the omentum or mesentery during this protracted period probably predisposes the tissues to hyporeactive vascular changes.

In some animals the compensatory changes were moderate in character and did not appre-

ciably curtail peripheral blood flow. Circulatory collapse occurred following the development of hyporeactivity with progressive suspension of intermittent arteriolar caliber changes and ultimate unresponsiveness to epinephrine.

In still others almost no compensatory vascular changes were noted. In these hyporeactivity was the factor to which the circulatory failure could be primarily attributed. Hyporeactivity developed early and was followed by a progressive deterioration of peripheral blood flow. Stagnation and pooling especially in terminal venous vessels were pronounced.

In addition to variations in response of individual animals as described, considerations must be given to differences which are introduced by changes in the experimental procedure. Fatal shock could be produced by any of a variety of tourniquet procedures involving 1, 2, or 4 limbs for periods of 4 to 12 hours. In general the compensatory changes accompanying fluid loss were accentuated with the increase in the mass of tissue subjected to tourniquet occlusion while decompensatory changes were accentuated by prolonging the period of tourniquet occlusion.

In taking a broad over all view of the syndrome all of these variations must be taken into account. Experimental procedures primarily concerned with obtaining a single reproducible type of shock for statistical analysis are deficient in that they tend to deal with only one aspect of the syndrome. In the present study stress is placed on hyporeactivity because of the tendency in the literature to overemphasize the fluid loss and attending vasoconstrictor aspects of the shock syndrome to almost complete exclusion of other factors.

The significance of the circulatory changes in the omentum and mesentery with respect to vascular changes in other visceral organs was brought out in the autopsy findings. Macroscopically at autopsy either an ischemic and pale condition or a congested and bloody appearance was found in the gut, liver, spleen, kidneys, and adrenals depending upon the corresponding tendency detected during the syndrome in the terminal blood vessels of the omentum and mesentery. The omentum and mesentery usually showed a tendency toward

congestion and stasis to a much lesser degree than was observed in the gut, liver and kidney at autopsy. Thus although the vascular changes in the omentum and mesentery do not by themselves materially contribute to the circulatory collapse they serve as an indication of the general direction of the changes occurring in other visceral structures.

As has been pointed out in a previous paper on irreversible hemorrhage shock (18) the development of hyporeactivity created a new problem with respect to therapy. Failure to respond to transfusion appears to be directly related to the development of hyporeactivity. The persistence of this hyporeactivity beyond a certain period of time renders fluid replacement therapy completely ineffective.

SUMMARY

Experiments were performed on dogs, cats and rabbits in which shock was produced under pentobarbital anesthesia by several different tourniquet procedures. The studies involved two methods. One consisted of continuous observations on specific physiologic reactions of the arteries, arterioles, precapillary sphincters, capillaries, collecting venules and veins of the exteriorized omentum or mesentery. The other consisted of testing blood samples removed at intervals during the shock syndrome. The serum was injected intravenously into normal rats and the effect on the arterioles and capillary vessels was noted in the exteriorized mesoappendix.

Tourniquets on 1 limb (cats and rabbits) and 2 limbs (dogs) for periods of 5 to 12 hours generally resulted in fatal circulatory collapse (20 out of 28 animals died). Three types of vascular response were obtained. Hyperreactive responses (compensatory) were accentuated when the tourniquet duration was less than 6 hours while hyporeactive responses (decompensatory) were accentuated when the tourniquet duration ranged from 7 to 12 hours. In some cases hyperreactive and hyporeactive patterns of response were equally prominent, the syndrome being characterized by an initial hyperreactive state followed by a hyporeactive state in which intermittent arteriolar caliber changes disappeared, the capillaries became filled with increasing amounts of blood.

the epinephrine response became subnormal and there occurred a partial relaxation first of the terminal arterioles and precapillary sphincters and later of the arteries and veins. In others the hyperreactive stage persisted throughout the greater part of the syndrome, hyporeactivity developing only during the last 20 to 30 minutes. In still others the hyperreactivity was relatively brief and was followed by a prolonged hyporeactive state.

Four limb venous occlusion for 3.5 hours produced fatal shock with an exaggerated hyperreactive pattern of response showing intense vasoconstriction and peripheral ischemia until 20 to 30 minutes before death. Fatal collapse with 2 limb venous occlusion for 4 hours showed a similar but milder response. One limb venous occlusion for 4.5 to 6 hours produced fatal shock in 3 of 4 cases. The hyporeactive state became more pronounced the longer the period of venous occlusion.

Of the 7 dogs whose hind legs were taped and then subjected to 6 to 7 hours of complete tourniquet application 4 went into fatal circulatory collapse. The nonfatal cases differed from the untaped controls in that the hyperreactivity to epinephrine was only slight and transient and little or no stimulation of vasomotion appeared. In the fatal cases hyporeactivity developed despite the curtailment of vasoconstriction and hyperreactivity.

Blood samples were taken at intervals during the shock syndrome and the serum injected into test rats. The humoral activity of the samples was determined by the reaction produced in the small blood vessels of the mesoappendix of the test rat. Control blood samples taken prior to tourniquet application had no effect on the reactivity of the rat vessels. Blood taken during the period in which the visceral circulation in the dog showed a hyperreactive pattern gave in the rat test a vasoconstrictor response. Blood taken during the intermediate period in which the hypernormal epinephrine responsiveness was falling and vasomotion was subnormal or absent gave as a rule in the rat test no demonstrable response. Blood taken during the period in which the visceral circulation in the dog showed a hyporeactive pattern produced in the test rat a vasodepressor response.

CONCLUSION

The initiating factor in the peripheral circulation is a reduction in rate and amount of blood flow. This occurs while the damaged limb is swelling and is associated with vasoconstriction and with hyperactivity of the terminal vessels as observed in the mesentery and omentum.

When the syndrome is fatal two sets of contributory factors are detected: an increased viscosity of the blood indicated by a rise in hematocrit and the development of hyporeactivity of the terminal blood vessels. The hyporeactivity occurred while the peripheral flow was still good and resulted in pooling of blood in the capillaries and venules, thereby intensifying the reduction in the circulating blood volume. In many cases hyporeactivity was the decisive factor in the syndrome.

Circulatory collapse in tourniquet shock is due to a reduction in blood volume caused by (a) loss of fluid into injured limbs and (b) sequestration of blood from the active circulation by pooling in the capillary bed and collecting venules. The latter is due to the development of a hyporeactive factor which progressively interferes with the peripheral vascular compensatory mechanisms.

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EFFECTS OF THE PARENTERAL ADMINISTRATION OF FLUIDS ON THE METABOLISM OF ELECTROLYTES DURING POSTOPERATIVE CONVALESCENCE

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THE therapeutic value of the intravenous administration of fluids during the course of any illness in which it has been difficult to maintain adequate fluid intake by mouth or in which the loss of fluid has been excessive is well established. However the administration of large amounts of fluid directly into the blood stream may occasionally produce unforeseen and inexplicable complications. Varying degrees of edema after repeated administration of fluids intravenously may be rationally explained as a complication of the sodium chloride and water which have been administered. After this obvious reason for edema has been evaluated such causes as malnutrition, loss of protein by drainage or hemorrhage, sepsis and impaired renal function may be given the etiologic credit they deserve.

Our interest concerning the intravenous administration of fluids pertains to certain practical aspects of therapy. Most of the literature on this subject suggests that a middle-of-the-road course be pursued when fluids are to be administered parenterally. For example one should administer a liter of physiologic saline solution and a liter of a 5 or 10 per cent solution of dextrose in distilled water or equal parts of these solutions. A patient who receives 3,000 cubic centimeters of a solution containing 0.45 per cent of sodium chloride solution or 1,500 cubic centimeters of physiologic saline solution during 24 hours receives 12.75 grams of sodium chloride which is 4 or 5 grams more sodium chloride than is ingested in the normal diet. A physiologic solution of sodium chloride however is the favorite solution for intravenous administration in spite of warnings concerning its injudicious employment. Coller

Dick and Maddock have shown that retention of water is a frequent occurrence after the administration of solutions of sodium chloride to patients who are very ill after surgical operation. However the parenteral use of isotonic solutions of sodium chloride possibly has become a habit because this solution may be a means of saving the lives of many patients who have an intestinal obstruction both before and after surgical treatment. Also there is abroad the general idea that intravenous administration of fluid produces a greater diuresis than does oral administration of the same amount of fluid. Of course the varying conceptions of the diuretic effects of oral versus parenteral administration of fluid is unimportant. No one would administer fluid intravenously in a case in which an adequate amount of fluid could be administered by mouth. Fantus has appropriately suggested that the intravenous administration of fluid produces less diuresis than does oral ingestion. Matas has emphasized what he considered the dangers of the administration of isotonic solutions of sodium chloride. It may be said therefore that the parenteral administration of isotonic solutions of sodium chloride is universal and that the procedure is not often complicated by any very grave untoward effects. The object of the present study was to determine if possible what changes occur in the excretion of the fixed bases and chlorides during the prolonged intravenous administration of isotonic solutions of sodium chloride (1 per cent) and solutions of dextrose (5 or 10 per cent) or mixtures of these solutions.

MATERIAL AND METHOD

The cases selected for study were those in which under ordinary circumstances large amounts of fluid would be administered intra-

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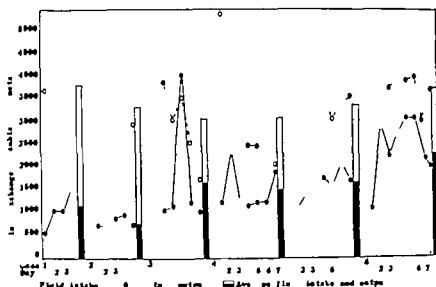


Fig. 1. Daily intake and output of fluid.

venously. They were all cases of carcinoma of the colon in all of the cases the involved segment of the colon had been resected. The usual postoperative treatment was not altered in any manner. Blood was collected within an hour after the operation and again at the conclusion of the study. The urine was collected and the total amount obtained in each 24 hours of the period of observation was examined. In Case 4 an indwelling catheter permitted the accurate collection of the specimens of urine. In the other cases the patients were often unable to micturate at the end of each day. However the total collections of urine during the periods of study were reasonably accurate. Vomitus and duodenal drainage were also collected. The one patient who passed feces during the period of study was given a tablespoonful of powdered charcoal at the end of the final period of 24 hours and all feces passed prior to the appearance of the charcoal were collected in one container. The results of the analysis of this specimen were included in the output for the last day (Case 3 6th day). Samples of the solutions of sodium chloride that were injected were analyzed and the composition was found to be almost uniform. The average composition of the analyzed samples served as a basis for computing the intake of sodium and chloride. The Ringer solutions administered in Case 5 were individually an-

alyzed. Aliquot samples of the various fluids which were given orally were mixed and analyzed. During the entire period of study the patient in Case 1 received only a 5 per cent solution of dextrose. If the dextrose that was administered parenterally was utilized, 1770 calories were thus administered. In Case 1. Similarly the patient in Case 2 received 1,120 calories in 5 days; the patient in Case 3 received 1,796 calories in 6 days; the patient in Case 4 received 3,207 calories in 7 days; and the patients in Cases 5 and 6 received 3,485 and 4,777 calories respectively in 8 days.

Samples of blood for the analyses were collected under oil in tubes containing heparin. The following analytical methods were employed for plasma sodium the method of Butler and Tuthill for plasma potassium, Hartzler's modification of the method of Shohl and Bennett for chlorides in plasma, the method of Keys for calcium in plasma, the method of Tisdall and Kramer for magnesium in plasma, the method of Denis. The amount of base contained in foods, feces, and urine was determined on ashed samples by means of the same procedures as used for the determination of the amount of sodium, potassium and magnesium in the blood plasma. The calcium was precipitated as the oxalate by a modification of the method of Washburn and Shear. The amount of chloride in the urine

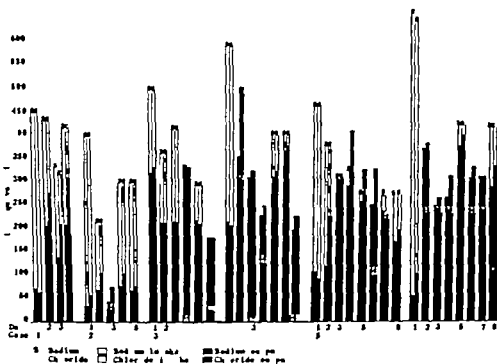


Fig. 2. Daily intake and output of sodium and chloride.

was determined by the open Carus method by means of reagents suggested by Peters and Van Slyke

RESULTS

The greater part of the fluid intake was given parenterally but toward the end of the period that each patient was being studied small amounts of water were taken by mouth as sips. Occasionally the sips consisted of fruit juices. When the fluid was fruit juice or other liquid food an aliquot was taken for analysis and the volume was included in the total intake. Figure 1 is a graphic representation of the daily intake and output of fluid. At the end of the period of study in each case is given an average of the daily intake and output of fluid. When a transfusion was given the total volume of blood was included in the fluid intake and the total amount of sodium, potassium, magnesium, calcium and chloride of the blood was added to the total intake of these substances. In one case (Case 5) the patient received Ringer's solution in the last 2 days of observation and the amount of base and chloride of this solution was likewise included in the results of the analysis of the intake. As is indicated in the graph the fluid output exceeded the intake only once and that was in Case 3 on the 4th day of the study. The

volume of the total fluid output is the sum total of the fluid lost in the urine by duodenal suction and on one or two occasions in vomitus. The total output of sodium, potassium, magnesium, calcium and chloride includes the amount of these substances lost in the vomitus, duodenal fluid and urine. The amount of fluid and electrolytes lost through sweating and respiration could not be accounted for in this study. The experimental work was done in cool weather. The losses of electrolytes through the sweat probably were not of very great importance.

The daily intake and output of sodium and chloride is shown in Figure 2. In Figure 3 the averages of the daily excretion of sodium and chloride are shown. Only in Case 4 did the average excretion of these substances exceed the average intake. Each individual displayed marked differences in the exchange of sodium. In Cases 1 and 2 (Fig. 2) the patients excreted a very small percentage of the total intake of sodium. At the end of the period of observation we were unable to account for 1,244 milliequivalents of sodium in Case 1 and 952 milliequivalents of sodium in Case 2. In Case 3 the patient apparently retained 636 milliequivalents of sodium during the first 3 days. However, during the 4th day 3,440 cubic

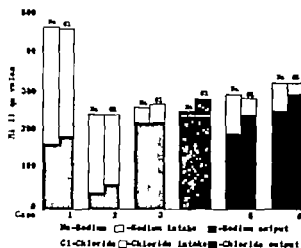


Fig. 3 Average daily excretion of sodium and chloride.

centimeters of a 5 per cent solution of dextrose were given intravenously 165 cubic centimeters of water were administered orally and 4,050 cubic centimeters of urine were excreted. This large volume of urine contained a half of the 636 milliequivalents of sodium which had been retained or were not accounted for. At the end of the 6-day period of observation however there were still 246 milliequivalents of sodium which were unaccounted for and thus probably retained. In Case 4 the excretion of sodium exceeded the ingestion of sodium by 38 milliequivalents during the 7 day period of study. The intake of sodium in this case was 39 milliequivalents which is 260 milliequivalents less than the average daily intake of 299 milliequivalents in all the cases studied. In Case 5 the patient excreted only 1,517 of the total 2,338 milliequivalents received which leaves 821 milliequivalents unaccounted for or retained. In Case 6 the patient maintained an output of fluid which was consistently higher than that excreted by any of the other patients, yet 483 milliequivalents of sodium were unaccounted for or retained at the end of the 8 day period of study.

Generally the intake of chloride was the same as the intake of sodium since the chloride salt of the sodium was administered parenterally. The excretion of chloride (Fig. 2) was not the same as the excretion of sodium except approximately in Case 3 (Fig. 2). In all of the other cases more chloride than sodium was excreted. The greatest loss of chloride was ob-

served in Cases 5 and 6 and this loss of output probably can be accounted for by the fact that in these 2 cases large volumes of fluids were removed by means of duodenal suction.

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The excretion of potassium seemed to be definitely increased during the first 4 post-operative days. This increased excretion of potassium is probably the same phenomenon observed by Gamble, Ross, and Tisdall and Benedict during fasting. They observed that in the early days of a fast the excretion of potassium was from two to three times greater than during equal periods later in the fast. Gamble, Ross and Tisdall expressed the opinion that increased excretion of potassium was related to a reduction in the stored glycogen and consequent loss of the intracellular water in which it had been dissolved. Silvette, Britton and Kline agreed with Gamble, Ross and Tisdall, concerning this increased excretion of potassium. Byrom found that the increased initial loss of potassium occurred if ample supply of carbohydrate was administered but could be prevented if both potassium and carbohydrate were given. A most important, but not a new conception of the loss of potassium was advanced by Thaler who observed that the excretion of potassium was increased if the intake of sodium chloride was increased. Sodium and potassium are closely related chemical bases and deranged concentrations in physiologic fluids or in fluids administered are liable to be accompanied by deranged excretions.

The intake of nitrogen was not determined. The nitrogen like potassium, was mainly included in the blood transfusion. The daily excretion of nitrogen varied from 2,370 to

15763 milligrams The excretion of nitrogen tended to be low during the first postoperative day and higher than the average during the 3 succeeding days.

Generally the concentrations of sodium potassium calcium magnesium, chloride hemoglobin and the hematocrit reading showed no great change.

In spite of the large intake of sodium and chloride (the intake of sodium averaged 299 milliequivalents per day in all cases) the concentration of the sodium and chloride in the plasma remained approximately constant or was reduced in all cases. It is of interest here to recall that considerable amounts of sodium were retained or unaccounted for in all cases except Case 4. The total concentration of base in the plasma paralleled that of the sodium and was generally slightly reduced. Reduction in the concentration of the hemoglobin and a decrease in the normal hematocrit reading were the rule and probably indicated that the blood had been diluted.

COMMENT

The patients observed in this study differ in several respects from one who is being starved. They all had had an anesthetic and an abdominal operation and fluids containing sodium chloride and solutions of dextrose were administered. However little nourishment was taken by mouth. In the first few days of starvation according to Gamble and his co-workers destruction of protoplasm with its attendant loss in body weight is accompanied by losses of intracellular and extracellular bases chiefly potassium and sodium and body water from the intracellular and extracellular compartments in such amounts that the base content of the plasma and extracellular fluids bathing the cells remains essentially unchanged. Our Case 4 was the only one in which we observed a negative sodium balance comparable to that seen in starvation. In the other 5 cases the patients apparently retained much of the administered sodium and the concentration of sodium in the urine was relatively low rather than high. At the same time the average volume of urine excreted during the 24 hour period by our patients was less than the optimal normal excretion of 1500 cubic centi-

meters. It seems evident therefore that the retained sodium in these cases was accompanied by an appropriately equivalent retention of water—a finding which is in harmony with the interpretation of numerous studies on the relationship between base and water metabolism. Much of the water injected was consequently not available for replacement of fluid lost by evaporation perspiration or in the urine which together should amount to about 3500 cubic centimeters in adults according to the standards proposed by Collier, Dick and Maddock.

That the foregoing conditions may not be optimal for the performance of normal physiologic functions by the kidneys is illustrated by the data obtained in Case 5. During the 8 day period of study 2338 milliequivalents of sodium were administered. Fifteen hundred and seventeen milliequivalents or not quite two-thirds of the sodium were excreted. The concentration of sodium in the urine increased until it reached 161 milliequivalents per liter on the 6th day. The concentration of sodium in the urine then diminished rapidly to 62 milliequivalents per liter on the 8th day. The specific gravity of the urine decreased from 1.023 to 1.008. We have observed that oliguria and practically an anuria can be produced by the administration of sodium chloride in cases in which renal function is decreased. The data in this study seem to indicate that the functional activity of the apparently normal kidney at times may be reduced greatly by the administration of sodium chloride. The impression that normal kidneys can be depended upon to retain what the body needs and excrete the excess is so nearly true that this belief may be dangerous. The elasticity of normal renal function is enormous. It should however be kept in mind that once any organ is overloaded fatigue may come on rapidly and prove disastrous.

The parenteral administration of physiologic saline solutions during intestinal obstruction in cases in which chloride has been lost produces such immediate benefits that one feels that physiologic solutions of sodium chloride are always safe to administer in large quantities. Nothing is farther from the truth. Certain fundamental facts must be kept in mind

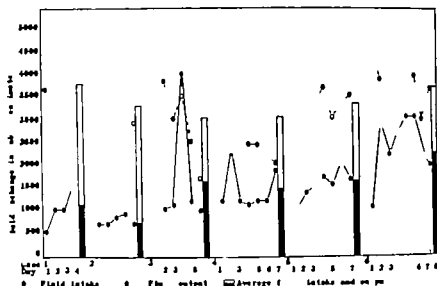


Fig. Daily Intake and output of field.

venously. They were all cases of carcinoma of the colon in all of the cases the involved segment of the colon had been resected. The usual postoperative treatment was not altered in any manner. Blood was collected within an hour after the operation and again at the conclusion of the study. The urine was collected and the total amount obtained in each 24 hours of the period of observation was examined. In Case 4, an indwelling catheter permitted the accurate collection of the specimens of urine. In the other cases the patients were often unable to micturate at the end of each day. However, the total collections of urine during the periods of study were reasonably accurate. Vomitus and duodenal drainage were also collected. The one patient who passed feces during the period of study was given a tablespoonful of powdered charcoal at the end of the final period of 24 hours and all feces passed prior to the appearance of the charcoal were collected in one container. The results of the analysis of this specimen were included in the output for the last day (Case 3 6th day). Samples of the solutions of sodium chloride that were injected were analyzed and the composition was found to be almost uniform. The average composition of the analyzed samples served as a basis for computing the intake of sodium and chloride. The Ringer solutions administered in Case 5 were individually an-

alyzed. Aliquot samples of the various fluids which were given orally were mixed and analyzed. During the entire period of study the patient in Case 1 received only a 5 per cent solution of dextrose. If the dextrose that was administered parenterally was utilized, 1,770 calories were thus administered in Case 1. Similarly the patient in Case 2 received 1,420 calories in 5 days; the patient in Case 3 received 1,796 calories in 6 days; the patient in Case 4 received 3,207 calories in 7 days; and the patients in Cases 5 and 6 received 3,483 and 4,777 calories, respectively in 8 days.

Samples of blood for the analyses were collected under oil in tubes containing heparin. The following analytical methods were employed for plasma sodium, the method of Butler and Tuthill for plasma potassium, Hartzler's modification of the method of Shohl and Bennett for chlorides in plasma, the method of Keys for calcium in plasma, the method of Tisdall and Kramer for magnesium in plasma, the method of Denis for the amount of base contained in foods, feces, and urine was determined on ashed samples by means of the same procedures as used for the determination of the amount of sodium, potassium and magnesium in the blood plasma. The calcium was precipitated as the oxalate by a modification of the method of Washburn and Shear. The amount of chloride in the urine

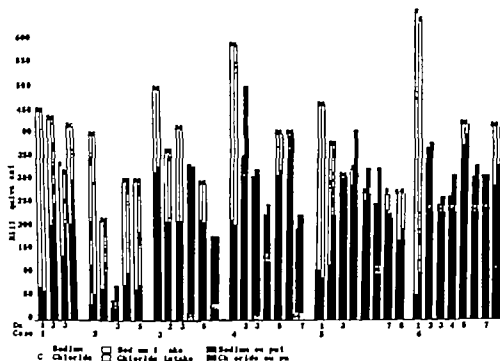


Fig. 2. Daily intake and output of sodium and chloride

was determined by the open Canus method by means of reagents suggested by Peters and Van Slyke

RESULTS

The greater part of the fluid intake was given parenterally but, toward the end of the period that each patient was being studied small amounts of water were taken by mouth as sips. Occasionally the sips consisted of fruit juices. When the fluid was fruit juice or other liquid food an aliquot was taken for analysis and the volume was included in the total intake. Figure 1 is a graphic representation of the daily intake and output of fluid. At the end of the period of study in each case is given an average of the daily intake and output of fluid. When a transfusion was given, the total volume of blood was included in the fluid intake and the total amount of sodium potassium magnesium calcium and chloride of the blood was added to the total intake of these substances. In one case (Case 5) the patient received Ringer's solution in the last 2 days of observation and the amount of base and chloride of this solution was likewise included in the results of the analysis of the intake. As is indicated in the graph, the fluid output exceeded the intake only once and that was in Case 3 on the 4th day of the study. The

volume of the total fluid output is the sum total of the fluid lost in the urine by duodenal suction and on one or two occasions in vomitus. The total output of sodium, potassium magnesium calcium and chloride includes the amount of these substances lost in the vomitus duodenal fluid and urine. The amount of fluid and electrolytes lost through sweating and respiration could not be accounted for in this study. The experimental work was done in cool weather. The losses of electrolytes through the sweat probably were not of very great importance.

The daily intake and output of sodium and chloride is shown in Figure 2. In Figure 3 the averages of the daily excretion of sodium and chloride are shown. Only in Case 4 did the average excretion of these substances exceed the average intake. Each individual displayed marked differences in the exchange of sodium. In Cases 1 and 2 (Fig. 2) the patients excreted a very small percentage of the total intake of sodium. At the end of the period of observation we were unable to account for 1,244 milliequivalents of sodium in Case 1 and 952 milliequivalents of sodium in Case 2. In Case 3 the patient apparently retained 636 milliequivalents of sodium during the first 3 days. However during the 4th day 3,440 cubic

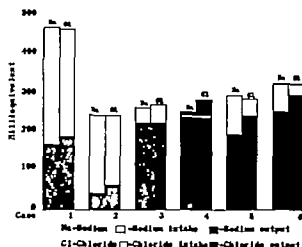


Fig. 3. Average daily excretion of sodium and chloride.

centimeters of a 5 per cent solution of dextrose were given intravenously 165 cubic centimeters of water were administered orally and 4,050 cubic centimeters of urine were excreted. This large volume of urine contained a half of the 636 milliequivalents of sodium which had been retained or were not accounted for. At the end of the 6-day period of observation however there were still 246 milliequivalents of sodium which were unaccounted for and thus probably retained. In Case 4 the excretion of sodium exceeded the ingestion of sodium by 38 milliequivalents during the 7 day period of study. The intake of sodium in this case was 39 milliequivalents which is 260 milliequivalents less than the average daily intake of 299 milliequivalents in all the cases studied. In Case 5 the patient excreted only 157 of the total 2,338 milliequivalents received which leaves 821 milliequivalents unaccounted for or retained. In Case 6 the patient maintained an output of fluid which was consistently higher than that excreted by any of the other patients, yet 483 milliequivalents of sodium were unaccounted for or retained at the end of the 8 day period of study.

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and no formula can be given to guide those who wish to ignore these facts. The average diet contains approximately 2 grams of sodium (equivalent to about 5 grams of sodium chloride) although one may take as much as 10 or more grams of sodium chloride daily. It is interesting to compare an intake of 10 grams of sodium chloride with the amount received by a patient who is given 3 000 cubic centimeters of physiologic saline solution intravenously. The patient receives about five times the average daily intake of sodium chloride required for the healthy adult and two and one half times as much as the individual who through habit has taken 10 grams daily. It is by ignoring these simple facts that patients who have not lost chlorides by vomiting by duodenal drainage or by extensive burns of the surface of the body often leave the hospital after surgical operations with a small amount of dependent edema, probably nutritional in origin."

SUMMARY

During postoperative parenteral administration of solutions of sodium chloride to patients who were not taking food considerable retention of sodium occurred in 5 of 6 cases. The concentration of base in the plasma did not change appreciably. The volumes of urine

were less than optimum, and 1 patient became unable to excrete concentrated urine, possibly as the result of the administration of too much sodium chloride. Under these conditions water must be retained with base and we wish to emphasize that water administered in the form of physiologic saline solution is not available for the important requirements of evaporation and perspiration.

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THE TREATMENT OF THROMBOPHLEBITIS

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THE disabling and sometimes disastrous consequences of venous thrombosis are well known to every physician. The etiology and resultant pathology of this condition have been subjects of varied opinions since John Hunter first described thrombosis as a sequel of phlebitis. The treatment has not changed much however as it has been little except symptomatic. During the past few years anticoagulant therapy has gained prominence in the treatment of thrombophlebitis and its associated complications.

The first of these substances used was heparin after its purification by Murray and Best. This substance however has certain inherent difficulties in regard to its use; it is expensive, must be given intravenously, frequent determination of coagulation must be done, its results are not predictable and its margin of safety appears to be narrow.

With the discovery of dicumarol¹ by Link (3) and his associates in 1940, an anticoagulant not presenting most of these difficulties was made available for the treatment of thrombotic phenomena.

Some investigators have tried dicumarol in the treatment of thrombophlebitis and have reported favorable results. On the other hand there has been some adverse comment about the use of anticoagulants in the treatment of thrombophlebitis. The main criticism according to DeBakey has been that the series of investigations are not adequate nor are the results sufficiently impressive to justify definite statements.

In an effort further to evaluate the use of dicumarol we have subjected all patients with thrombophlebitis to a uniform type of therapy.

This series consists of 67 cases of thrombophlebitis and its complications. We have arbitrarily divided the cases into four groups:

This work was done under a research grant from the Wm. G. Kaeser Fund, Lenox Hill Hospital.
Technical assistance and procedure by Miss Ruth Lipkin, A.B.
Dicumarol furnished by Dr. G. R. Hazel of Abbott Laboratories.

on an anatomical basis. These consist of (1) superficial phlebitis, (2) deep phlebitis, (3) superficial and deep, (4) pulmonary embolization with or without a demonstrable phlebotic site.

The treatment and results for each group are discussed separately. Prothrombin times were done daily. The technique using the method of Shapiro with modifications is indicated below.

TECHNIQUE

1. Remove lung from freshly killed rabbit.
2. To remove blood, wash lung for about 15 minutes in cold running water. Blot out excess with filter paper.
3. Cut in small pieces, place in evaporating dish.
4. Place dishes in desiccator (Drying agent barium dioxide). Attach to suction apparatus to form a vacuum for about 10 to 15 minutes.
5. Place desiccator in incubator at 37 degrees for 24 hours. (Drying process).
6. Remove pieces of lung from desiccator, grind finely in mortar.
7. Keep in refrigerator (Good about 4 weeks.)

THROMBOPLASTIN

1. To 100 milligrams of rabbit's lungs (thromboplastin).
2. Add 5 cubic centimeters of normal physiological saline (0.8%).
3. Inactivate thromboplastin for 10 minutes in water bath at 57 degrees C. Stir constantly.
4. Remove from water bath and stir until thromboplastin reaches room temperature.
5. Add 5 cubic centimeters of calcium chloride (1:11 gr to 500 c.c.). Shake thoroughly.
6. Centrifuge for 4 minutes at 1800 revolutions. Use supernatant fluid.

OBTAINING BLOOD SPECIMEN

Using 20 gauge needles take 4-5 cubic centimeters of blood to 0.5 cubic centimeters of sodium oxalate (1:34 to 100 c.c.). Centrifuge, remove plasma.

PROTHROMBIN DETERMINATION

1. Place plasma in water bath kept at a constant 38 degrees temperature.
2. In small tubes add 0.2 cubic centimeter of thromboplastin.
3. To thromboplastin add 0.1 cubic centimeter of whole plasma. Start stop watch immediately. Use

a wire loop to pick up complete clot when it is formed
Record time of result.

SUPERFICIAL PHLEBITIS

In this group there are 11 cases 8 female and 3 male. The ages varied from 25 to 61 years 4 were postpartum 2 antepartum and 5 were cases of phlebitis of long standing unassociated with any known etiological factor. All of these patients were treated in the same fashion. Dicumarol was administered in sufficient dosage to keep the prothrombin time prolonged to double the normal value of that particular patient.

Wet boric acid dressings were applied continuously to the affected area and $\frac{1}{8}$ grain papaverine was given at irregular intervals for excessive pain. The average number of days in bed was 10 and the criteria taken for remission of the attack were diminution or disappearance of pain or tenderness over the affected areas, as well as normal temperature and pulse. Dicumarol was discontinued when these conditions were fulfilled and the patient was then allowed out of bed and active motion, usually with the application of an Ace bandage encouraged. The average total dose of drug was 1000 milligrams.

These patients have been followed for an average of from 6 to 10 months with no further recurrences reported to date. It is interesting to note that Case 7 had had repeated attacks of phlebitis during the past 10 years, each lasting from 3 to 4 months. This patient was out of bed and feeling well in 9 days and has had no further symptoms. Two interesting cases, especially from the standpoint of the obstetrician, Cases 1 and 10 in this group, were 2 antepartum patients who developed severe superficial phlebitis during the 7th and 3d months of pregnancy respectively. Patient 1 had marked tenderness and redness along the course of almost all the superficial veins of the thigh. No primary site of infection could be found. The patient was immediately started on the aforementioned regimen. On the 4th day when the patient was in the therapeutic range she was entirely free of pain for the first time. By the 10th day she was completely asymptomatic, and then was allowed out of bed. She was followed through-

out the rest of her pregnancy and did not develop recurrence of phlebitis. Two months later she delivered a normal male child. There was no excessive bleeding at the time of delivery and the baby showed no untoward effects due to dicumarol. The patient was followed during her postpartum course but showed no signs of phlebitis. The other patient also showed good response but had not reached term at the time of this report.

Although this series of cases is small, they are representative of the type of superficial phlebitis usually observed. The rapidity of response to therapy and the long remission encourages one to continue further therapy along these lines. It is further interesting to note that in none of these cases was there an attempt to control infection *per se* with either chemotherapy or other antiseptic agents.

DEEP PHLEBITIS

This group contains 27 patients. Nineteen of these were females 8 males. The ages varied from 18 to 67 years. Four of these patients were postpartum 16 were postoperative and the 7 remaining without any etiological factor. All of these patients were treated in the same way. Dicumarol was begun as soon as the diagnosis was made. The involved extremity was elevated, a cradle placed over the limb, and an ice bag applied to the point of maximum tenderness. The method of administering dicumarol was the same as described and prothrombin times were done daily. The largest dose administered was 2300 milligrams. The smallest was 500 milligrams. The criteria for remission were normal temperature and pulse, lack of tenderness over the affected veins as well as loss of pain and marked decrease in the amount of swelling. When these criteria were fulfilled the patient was allowed out of bed and an elastic stocking or an Ace bandage was applied. The prothrombin time was kept within the therapeutic range for at least 24 hours after patient got out of bed.

Under this regimen the average time in bed was 10.5 days with a range of 5 to 23 days. Pain usually subsided within 24 hours after the patient's prothrombin time was in the therapeutic range. Little if any sedation was needed during the rest of the course. Most

significant is the fact that there were no episodes of pulmonary embolization. The thrombotic process appeared to remain localized. No untoward effects from dicumarol occurred. In Case 13 the prothrombin time went as high as 70 seconds but there was no evidence of hemorrhagic phenomena.

SUPERFICIAL AND DEEP PHLEBITIS

There are 9 patients included in this group, 7 of which were female and 2 male. The age distribution was from 30 to 72 years. Five cases were postoperative hysterectomies, 1 was an antepartum patient in her 8th month and 3 were phlebitis without any known etiological factor. The regimen followed in these cases was the administration of dicumarol as here outlined above, elevation of the leg, wet boric acid dressings to the affected area, and papavarine in doses of $\frac{1}{2}$ grain every 4 hours for pain. The largest total dose administered in these cases was 1400 milligrams and the smallest 600 milligrams.

These patients remained in bed for an average of 14.7 days with a range of 7 to 25 days. There were no complications referable to embolic phenomena nor were there any toxic effects due to dicumarol. Patient 1 was a primipara who developed redness and a slight swelling over the medial aspect of the lower extremity just below the knee. There was marked tenderness over the short saphenous vein. The regimen outlined was initiated and the symptoms subsided within 7 days. This patient was delivered of a normal male child 2 months later. There were no concomitant hemorrhagic phenomena.

The second interesting case, Case 2, was a patient 72 years old. He had had a chronic phlebitis for the past 10 years. There was definite evidence of superficial and deep phlebitis. The regimen outlined was instituted and the patient was kept under therapy for 15 days. There was apparent subsidence of phlebotic symptoms and therapy was discontinued. The follow up course showed persistent edema. Three weeks later this patient suddenly went into coma and died despite supportive therapy. An autopsy showed fresh thrombosis throughout the iliac veins involving the vena cava.

Patient 7 was admitted in 1936 for a salpingo-oophorectomy. Eight days following the operation she developed deep phlebitis of the lower extremity and 10 days later a pulmonary embolus. She remained in the hospital for 3 months on symptomatic therapy. She was readmitted in 1939 with swelling of the leg as well as pain in chest, cough and blood tinged sputum. The diagnosis at this time was recurrent phlebitis with pulmonary embolism. From 1939 to 1943 this patient was seen on numerous occasions in the clinic, complaining of pain and swelling in one lower extremity. She had had various forms of therapy including application of leeches, cold compresses, elevation of the part, with little result. In 1943 she was admitted to the hospital for repair of ventral hernia. This time she had a slight swelling of the left lower extremity, with tenderness and redness along the medial aspect. The usual regimen was begun. Patient was kept on dicumarol for 16 days. This time the prothrombin time was allowed to return to normal and the ventral hernia repaired. On the 3d postoperative day dicumarol was again begun and she was kept in therapeutic range for the next 10 days. She was discharged with no symptoms of active phlebitis.

PULMONARY EMBOLIZATION

This group includes 10 patients, 7 of which were female and 3 male. Age distribution varied from 28 to 65 years. There was no previous history and there were no symptoms of phlebitis in any of these cases, the first symptoms being those referable to embolus of the lung. Eight of the patients had one pulmonary embolus while 3 had two episodes. These patients fit into the group described by Homan as silent thrombophlebitis in which the first symptom is referable to the embolus and not to the original phlebotic site. In 8 of the patients the conditions were postoperative, each patient having had some type of pelvic operation. The most obscure case was that of a 65 year old woman who had a typical episode of pulmonary infarction of unknown etiology.

All patients were treated in the same fashion. Dicumarol was begun as soon as the pa-

tient was seen and continued in sufficient doses to keep the prothrombin time elevated to twice its normal value. The only other therapy was an adequate amount of sedation to control pain.

While under therapy none of these patients had any further episodes of pulmonary emboli. This held true even for those who had more than one previous episode. These patients remained in bed an average of 14 days the longest time being 20 the shortest 13. One patient was found to be resistant to the ordinary dose of dicumarol. The prothrombin time in this case was never raised above 25 seconds. When a second group of pulmonary emboli occurred she was treated with heparin.

The results in this group of patients were fairly uniform while under treatment. There were no toxic effects due to dicumarol, and the drug was administered and controlled without difficulty.

SUMMARY

The above presentation not lending itself to statistical analysis indicates some interesting points in the therapy of phlebitis.

The diminution in the length of time of treatment, the lack of complications referable to phlebitis as well as to dicumarol make this form of therapy worthwhile. None of these cases while under treatment or in the post-treatment period developed emboli. In those cases, having had previous embolic phenomena, there was no further evidence of it after therapy was begun. Further in none of the 67 patients did other foci of thrombophlebitis occur either in the treatment or posttreatment periods.

Pain which is an outstanding feature of thrombosis, is markedly decreased in direct relationship to the initial elevation of the prothrombin time i.e. when the patient is in the therapeutic range the amount of sedation needed is markedly diminished. This very interesting feature was first pointed out by Zucker.

In contrast to other types of anticoagulant therapy dicumarol appears to have a wider margin of safety. Prothrombin time in these cases varied between 15 and 70 seconds. Despite this marked prolongation of the pro-

thrombin time there was no evidence of hemorrhagic diatheses.

We must not, however, develop a false sense of security in this wide margin of safety: each individual varies in his response to a given dose of dicumarol. Consequently prothrombin times must be done daily or at least preceding the administration of any given dose. Reference to the tables of any group of patients presented will indicate that despite the uniformity of the initial doses, subsequent doses varied markedly.

The initial doses consisted of 300 milligrams the first day and 200 milligrams the second day. Following these doses from 20 to 200 milligrams in 24 hours were given. To guide to the proper dose was the prothrombin time. If after 500 milligrams the prothrombin time had risen to double its initial value a further dose was given. If it was rising rapidly but had not reached the therapeutic range i.e. double its initial value no dose was given. If there was no rise or it was rising slowly from 50 to 200 milligrams was given depending upon the initial elevation. This scheme was followed throughout the course.

Under this regimen there usually was latency of 24 to 72 hours before the prothrombin time was affected. One must be wary of overdosage during the latter part of the latent phase. The third dose in our cases was almost always 100 milligrams.

Of the patients treated there were 37 treated for postoperative sequelae: 22 were antepartum and postpartum cases, and 15 were phlebitis cases without known etiological association. Dicumarol was begun during various intervals of the postoperative period, but in no case was it necessary to begin treatment before the 3d postoperative day. As far as could be determined there was no interference with wound healing and no hematomas developed. In the obstetrical cases, 19 of which were postpartum there was no increased vaginal bleeding nor was the postpartum period affected in any way. In these cases dicumarol was begun as early as 24 hours following delivery. Three antepartum patients had normal deliveries, one of these having received dicumarol in the last month of the third trimester.

In these series only one resistant case was encountered and her prothrombin time did not go above 20 seconds despite a total dosage of 2100 milligrams.

We have had little experience with other methods of treating thrombophlebitis, such as paravertebral procaine sympathetic block or venous section with ligation. This latter procedure was used in one case of deep phlebitis of the femoral vein combined with anticoagulant therapy. However the lack of complications due to either the thrombophlebitis or dicumarol would seem now to make anticoagulant therapy alone the procedure of choice.

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THE SURGICAL ANATOMY OF THE FACIAL NERVE

With Special Reference to the Parotid Gland

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ALTHOUGH the incidence of parotid tumor may be as low as 0.06 per cent (Sistrunk, 1921) treatment of the lesion is fraught with such difficulty that any aid offered by anatomy to the surgeon, would be of value. While injury to the facial nerve is not vitally damaging the resultant cosmetic deformity brings great psychic distress to the patient. In an attempt to avoid the latter effect roentgen therapy has often been resorted to in the management of these tumors. Bailey (1941) arguing for total parotidectomy calls attention to the radioresistance of most of the tumors; he also mentions the great tendency to recurrence because of the technical difficulties involved in the operative procedure. McFarland (1933) in studying over 400 cases, reported a 30 per cent recurrence of parotid tumors locally removed especially those of smaller size.

Many authors have discussed the surgery and pathology of the parotid area, but relatively little has been written about the exact relation of the gland to the facial nerve. The most extensive anatomic study of the nerve (Tortella, 1935) is based upon only seven specimens. The purpose of the present study therefore is to furnish such information on the nerve and parotid gland accumulated from a large series of specimens.

MATERIALS AND METHODS

The series herein reported upon consists of 100 facial halves selected from specimens in the anatomical laboratories of Northwestern University Medical School.¹ The specimens were adult whites and negroes (79 white, 21 negro) mostly male (82 males, 18 females). Only specimens with complete dissection of the facial nerve were included. No attempt was made to study bilateral configurations.

A fixed method of exposure was followed, devised to preserve the relationship of the gland to the nerves. The skin and superficial fascia over

the parotid area were carefully removed, from posterior to anterior. The free anterior border of the parotid gland was then mobilized, and a careful search was made for the emerging branches of the facial nerve, particularly the temporal and zygomatic portions. The mandibular and cervical divisions were next uncovered along the anterior-inferior border of the gland. These divisions being used as guides, the dissection was then carried into the gland itself. In virtually all instances, a natural cleavage plane was found to exist between the lobes of the gland which allowed the dissection to locate the main trunk of the nerve at its point of division. Careful individual drawings of the area were then prepared to show the configuration of the main portions of the nerve and the anastomoses between its adjacent divisions and branches.

In the greater number of the specimens (66) the distance between the point of bifurcation of the nerve and the external angle of the mandible was recorded (Table I). In 75 specimens the height and width of the parotid gland were measured, and the shape recorded. The presence or absence of accessory glands and the general configuration and course of the main parotid duct were also noted.

All of the illustrations were prepared from specimens selected from the series.

OBSERVATIONS AND DISCUSSION

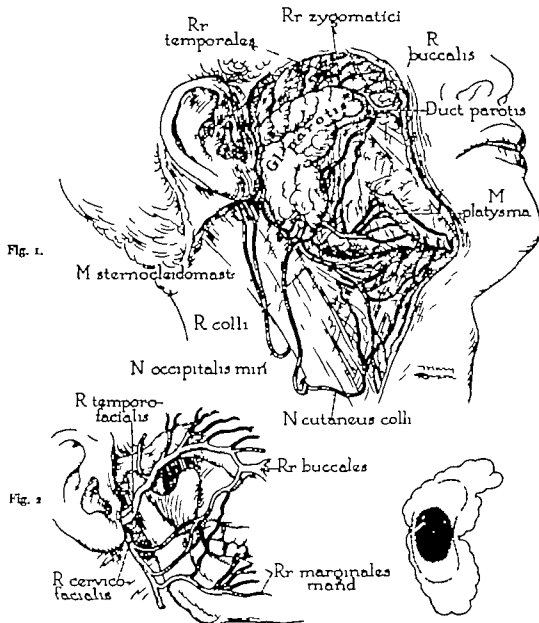
Developmentally the relationship of the parotid gland to the facial nerve is a secondary one, since the gland migrates backward from its original site of pharyngeal outpouching. Controversy however has developed as to the mode of formation of the lobes of the gland. Grégoire (1911)

TABLE I.—HEIGHT OF NERVE ABOVE
ANGLE OF JAW

Height cm	Number	Height cm	Number
1.4-1.69		3.2-3.49	1
7-99	0	3.5-3.79	20
2.0-2.99		3.8-4.09	8
2.2-2.59	5	4-4.39	5
0-2.89	7	4.4-4.69	
2.0-3.9	9	Average—3.4 cm.	66

¹Contribution from Anatomical Laboratory of Northwestern University Medical School.

Approximately 30 additional specimens were examined although imperfect in respect to some details of nervous branches; their general structure would support all statements made hereinafter.



Figs. 1 to 3. Facial nerve and parotid gland superficial and deep dissections. Adult male, negro. Showing the divisions and ramification of the nerve and their relation to the gland, and to the mandible and zygomatic arch. In Figure 3, lower right, the margin of the deep lobe (broken line) and isthmus (cross-hatching) are shown diagrammatically.

from a study of 60 adult and 8 fetal glands, concluded that the deep lobe was formed by a migration of a portion of the superior pole of the gland the latter retaining connection with the superficial lobe which remained situated above the facial nerve. McWhorter (1917) from an examination of 66 adult parotids and 16 in fetal and newborn specimens, was, on the contrary, of the opinion that the gland was H-shaped with the connecting arm (or isthmus) between the two diverging portions of the facial nerve. Rouvière and Cordier (1934) after reconstructing two glands, came to the conclusion that both Grégoire and McWhorter were correct. In the 31 millimeter fetus the gland

was found to be entirely superficial, while in the 51 millimeter fetus there were projections which passed over the facial nerve superiorly as well as some which passed between the two portions of the nerve to form a deep lobe.

The present authors found that the general relationships which were described by McWhorter were recognized in their specimens. The facial nerve, lying between two lobes of the parotid partially separates the gland into a large superficial and a small deep portion, the two parts being connected by a slender isthmus which passes between the two diverging portions of the nerve (Fig. 3).

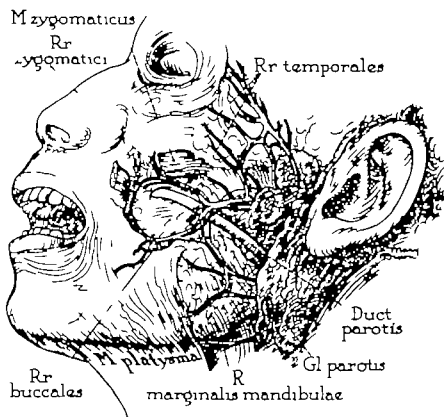


Fig. 4.

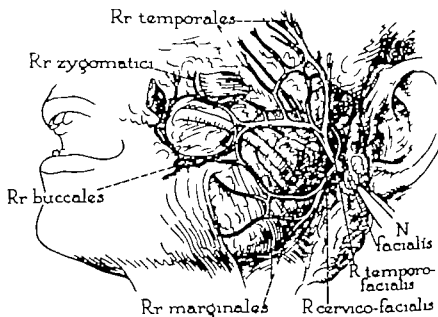


Fig. 5.

Figs. 4 and 5. Facial nerve superficial and deep dissections. Adult male negro. Showing secondary anastomosis between the main divisions. The secondary loop sur rounded the isthmus (transected)

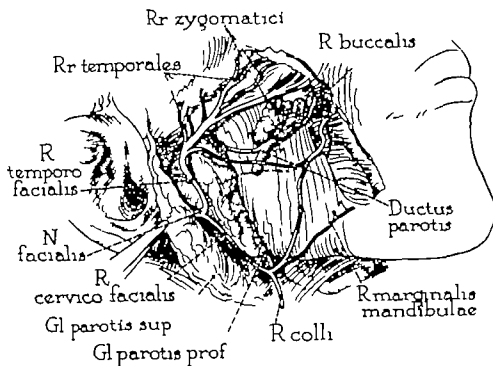


Fig. 6.

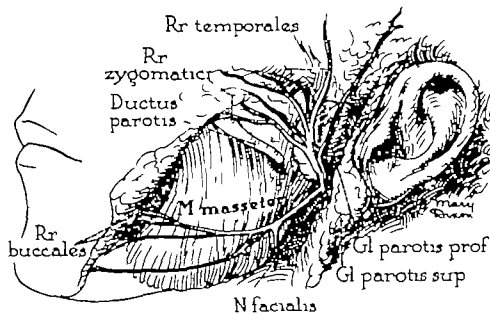


Fig. 7

Figs. 6 and 7 Facial nerves, deep dissections. Adult male, white. Figure 6 relation of the nerve and its divisions to the "leaves" of the parotid gland. Figure 7 demonstrating the relation of the nonanastomotic type of nerve to the zygoma, mandible and masseter muscle. In Figures 6 and 7 the parotid duct has been cut.

A Facial Nerve

After the facial nerve emerges from the skull through the stylomastoid foramen, it passes inferiorly with slight anterolateral inclination to plunge into the substance of the gland. With the exception of one or two small muscular rami all of its branches are given off after it has entered the parotid. Regularly the single main trunk splits

into two principal divisions, the temporofacial and cervicofacial portions. The point of bifurcation occurs 5 to 7 millimeters dorsal to the ramus of the mandible, where the nerve is entirely surrounded by glandular tissue. In 66 specimens it was found to be a distance of from 1.4 to 4.7 centimeters above the external angle of the mandible, measured along the palpable posterior border of

the ramus (Table I). Most of the specimens fall in a group between 2.9 and 4.4 centimeters (an interval distance of 1.5 cm.) the average measurement is 3.4 centimeters. Converted into a rough measurement of surgical value, the point of bifurcation of the facial nerve lies posterior and slightly medial to the ramus of the mandible and superiorly two-thirds of the distance between the external angle of the mandible and the palpable condyloid process (temporomandibular articulation). Much of the absolute variation in distance is explained on the basis of comparative head size: the greater the cranial and mandibular development, the greater will be the interval.

Of the two principal divisions of the facial formed at the point of bifurcation, the temporo-facial portion, supplying the upper part of the face is by far the larger (Figs. 1 to 7). It is often two to three times the size of the cervicofacial component. The upper division courses anterosuperiorly just below the upper border of the parotid gland. In the first part of its course it lies between the two lobes of the gland (see hereinafter). The lower division arches downward between the two lobes in close association with the posterior border of the ramus of the mandible.

The pattern of branching from the two main divisions which is described in anatomical text books, was found to occur infrequently in the authors' specimens. However the temporal zygomatic, buccal, mandibular and cervical rami (named on the basis of regional supply) were always identifiable. The scheme of origin, however, varied, and to such an extent that eight general types of configuration could be distinguished (Fig. 8 I to VIII). For purposes of convenience in discussion, these were arranged in the order of increasing complexity beginning with the simple type regularly described and figured in anatomical textbooks, and ending with those which exhibited a markedly plexiform arrangement. Between these extremes were placed several groups the selection of which was based upon the number of large anastomoses between branches of one of the two principal divisions of the nerve (preponderantly associated with the temporal portion)¹ and upon the number of anastomoses between the cervicofacial and temporo-facial divisions of the nerve. Some of the anastomoses occurred within the gland others beyond its margins.

Type I (13 specimens, 8 left and 5 right). The basic plan of nerve Type I is simple (Fig. 7 cf. Fig. 8, I). No large unions occur between the various portions of the nerve rami arise in a spray and diverge from the two primary portions

as blades leave the handle of a fan. Within the substance and close to the border of the parotid gland these fibers are, relatively speaking, of considerable caliber (diameter 2.0 mm.). They vary in number from four to six at the point of emergence from the gland. The nerves of the temporal supply emerge from the superior border of the parotid and arch anteriorly and cranially to join the musculature of the ocular and temporal regions. The zygomatic ramus, which often includes the buccal supply courses transversely across the face just above the parotid duct, or crossing it. Either this branch, or more commonly the temporal division, is very large in comparison with the remaining branches. The inferior directed cervical and mandibular rami remain hidden between the two lobes of the gland, to emerge finally from the lower pole. The mandibular branches follow along the body of the mandible, or just inferior to it. It is this branch that several surgeons (Bailey, Adson, and Ott) identify first in preparation for total parotidectomy. The cervical portion passes into the platysma muscle. The single exception to this method of distribution is represented by those specimens of Type II (4 number) in which a component of the buccal supply passes transversely across the maxillary bone on a level with the angle of the mouth. This buccal component is a very slender fiber and is readily found in dissection.

Type II (11 specimens, 5 left, 6 right). A distinguishing characteristic of Type II is the presence of a single anastomosis between various components of the temporo-facial division (Fig. 8, II). In virtually all of the representatives of this group the temporo-facial division quickly splits into two large rami, one directed anterosuperiorly and the other passing anterosuperiorly. The latter soon further subdivides into temporally directed branches to the muscles below the eye and a more transversely directed ramus. The middle and lower rami then anastomose at a point 1 to 3 centimeters beyond the anterior border of the gland from the loop thus formed given off numerous fine twigs to the buccal zygomatic musculatures, and less frequently the temporal region.

In most instances this anastomosis is intimately related to the parotid duct, lying just superior to it. Rarely (2 cases) the communication occurs within the substance of the gland. From the connecting stem spring the temporal and zygomatic rami, which (as in Type I) are already separated as they pass from the border of the gland. Most frequently (one instance) the intraparotid loop passes around the superficial temporal artery

¹A fact first noted by Turella (1931).

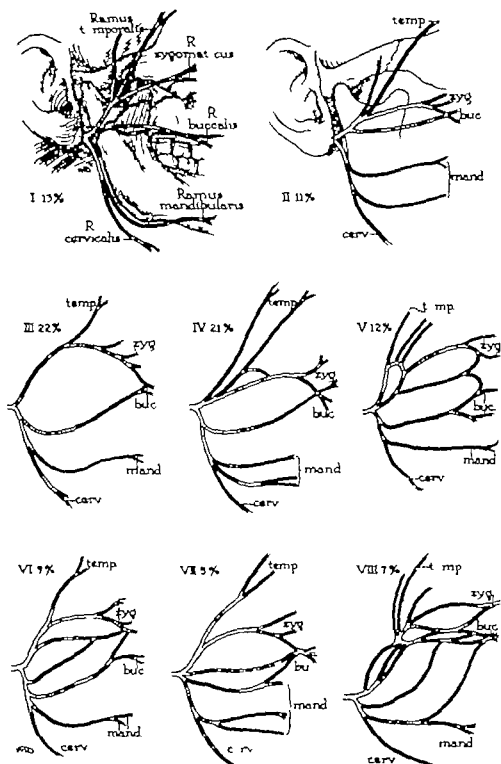


Fig 8 Major types of facial nerve branching and anastomosis. I Major divisions (temporal and facial) independent II anastomosis between ramal of the temporal division III connection between adjacent ramal from the major divisions IV anastomoses representing a composite of those in II and III V proximal anastomosis within the temporal component, distal interconnection between the latter and the cervical component VI, two anastomotic ramal sent from the buccal division of the nerve, contributing to the zygomatic part of the temporal VII transverse ramus from the trunk of the nerve, contributing to the buccal ramus formed by anastomosis between the two major divisions VIII richly plexiform communications, especially within the temporal portion of the nerve.

vein. The inferiorly directed branches in specimens of Type II are similar to the corresponding rami of Type I.

Type III (22 specimens, 9 left, 13 right) This is the third of the groups in which the pattern of configuration of the nerve is of basic character. In the scale of ascending complexity it represents the first intermingling of elements derived from both of the primary divisions of the nerve, namely the temporofacial and cervicofacial portions (Fig 6 and Fig 8, III). A slender trunk arises from the cervicofacial division very quickly after its origin from the main nerve (within 1.5 cm.) and passes superiorly in an oblique course to anastomose with a strong, arching continuation of the temporofacial division (Figs. 1 to 3). In all instances the anastomosis is extraglandular occurring most frequently 1 to 3 centimeters beyond the anterosuperior extremity of the gland. In most instances the anastomosis occurs immediately over the parotid duct, just before the latter passes deeply to pierce the buccal muscles.

In an exceptional specimen (Figs. 1 and 2) the contribution from the cervicofacial division was formed by the union of several filaments.

Type IV (21 specimens, 11 left, 10 right) Type IV is essentially a composite of the two preceding patterns. There is an anastomosis between the temporal and zygomatic subdivisions of the main superior trunk as well as one between the superiorly directed ramus from the cervicofacial division and a strong branch from the zygomaticobuccal supply (Figs. 4 and 5 and Fig 8 IV). In 6 cases the anastomosis occurring within the temporofacial portion of the nerve was intraglandular while in the remaining 15 the union occurred beyond the anterior border of the parotid. In 20 cases the anastomosis between the two principal divisions was extraglandular i.e. having relationships similar to those obtaining in Type III. In the remaining single instance the anastomosis lay between the two leaves of the gland. The latter was the only case among the representatives of Type IV in which both of the anastomoses were entirely intraglandular.

Type V (12 specimens, 6 left, 6 right) In specimens belonging to this group one characteristic feature is the presence, in the temporofacial division of the nerve of two large anastomoses (Fig 8 V). The proximal loop is very small and intraglandular. It is usually about 1.5 centimeters in diameter and often encloses the temporal artery and vein. From it arise three major components: small temporal filaments to the muscles at the orbit; a heavier superior branch to the zygomatic musculature; a smaller some-

what inferior branch which forms a second loop by joining the preceding over the parotid duct at a point 1 to 3 centimeters distal to the anterior pole of the gland. As the second of two characteristics, this third component is reinforced by an anterosuperior contribution from the cervicofacial division (within a distance of 1 cm. from its origin in the main trunk of the nerve). In this way the two main components of the nerve are brought into anastomotic connection. From this distal loop, formed by junction of the two main divisions, small filaments pass the musculature above the angle of the mouth. In only one instance is lower communication was entirely intraglandular; in the remaining 11 the cervicofacial contribution passed beyond the margin of the gland below union.

Type VI (9 specimens, 3 left, 6 right). The pattern in Type VI is the converse of the preceding, in that the arrangement of major and minor loops is reversed. One variable anastomotic loop occurs between rami of the temporofacial division (Fig 8 VI). In 5 cases, it was relatively small and entirely intraglandular as in the case of the proximal loop in Type V. In 2 cases it extended less than 2 centimeters beyond the anterior border of the superior portion of the gland. In the remaining 2 (of the total 9) it extended approximately 1 centimeter beyond the border. Additionally Type VI possesses two anastomotic filaments which pass from the cervicofacial division to intermingle with elements of the temporofacial portion. In 2 instances, these branches arose by a very short common trunk from the cervicofacial division, approximately 1 centimeter beyond the latter's origin. In the remaining 7 a proximal ramus arose about 1 centimeter from the main bifurcation, and a second one was given off at a distance of from 2 to 3.5 centimeters beyond the bifurcation. In 3 cases the latter branch crossed the angle of the jaw. In all instances the ramus which arose from the inferior division joined the same transversely directed branch, in succession, 1 centimeter apart to form an arcade with a small so that the additions gave the appearance of reinforcing it. From the distal loop, which usually lay over the anterior border of the masseter muscle, numerous small filaments passed to superior labial and zygomatic musculature.

Type VII (4 specimens, 1 left, 3 right). The seventh type, while not strikingly complex, was the least common configuration encountered in the entire investigation. It is very similar to Type III in that anastomosis occurs between a strong transverse branch of the temporofacial

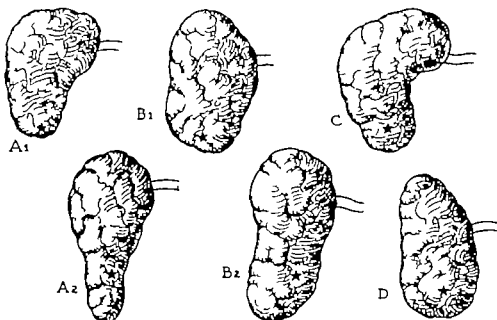


Fig. 9. Types of parotid gland, recording variations in form and size. Star in each indicates the site of the external angle of the mandible.

division with a smaller ascending ramus of the cervicofacial portion of the main nerve (Fig. 8 VII). The unique feature is the presence of a central branch arising from the main trunk of the nerve and passing transversely to join the above mentioned anastomosis. In this way a third element is contributed to the primary anastomosis. From the anastomosis formed by the union of three branches numerous terminal filaments arise to supply the musculature between the lower eyelid and the angle of the mouth. The anastomosis bears the usual intimate relationship to the parotid duct but the point of union is usually situated just inferior to the duct.

Type VIII (7 specimens, 3 left, 4 right) Specimens in this group are characterized by the presence of richly plexiform intercommunications (Fig. 8 VIII). None has a strong transverse branch such as was so commonly present in specimens belonging to the other groups. From 4 to 7 intercommunications occur within the nerve itself most often between the two main divisions. What the individual rami lack in size they make up for in number and in frequency of intercommunication. A second striking feature is the presence of small triangular masses of fibrous tissue which occurs between adjacent branches of a nerve. Two of these were found at the first or second branchings of the temporofacial division. They were firmly attached and appeared to be an integral part of the main nervous structure. It is the authors belief that the presence of such a plexiform arrangement is responsible for the

partial successes reported by Duval and Redon (1932) who removed the cervicofacial portion of the nerve in the course of total parotidectomy¹

B. Parotid Gland

The parotid gland is an organ of variable form. Despite this fact the variations can be rather satisfactorily classified (Fig. 9). In addition to the criterion of size, there is that of relative bulk of the superficial and deep portions as discussed by other authors (Grégoire 1912; McWhorter 1917). This relationship is also variable since the deep lobe may be merely a small button of glandular tissue, or may come close to equaling in size its overlying superficial lobe.

The features of form and size were combined in studying 76 glands. The main grouping was made on the basis of form while subgroups were based upon size. The larger glands (those longer than 6 cm.) extend for a distance of several centimeters into the neck just anterior to the ventral border of the sternocleidomastoid muscle—a fact which is of surgical interest.

Length of gland varies between 4.5 and 9.2 centimeters (average, 6 cm.) while the width varies between 2 and 5.4 (average 3.3 cm.) More than half of the glands (40 specimens or 52.6 per cent) fall into a group for which a conventional textbook description would be suitable: they are triangular in shape, largest at the superior extremity and narrowing gradually to a blunt apex.

¹In 5 cases, patients had mouth droop, and had some involvement of the eye; the other 3 were esthetically successful.

pointing inferiorly. Within this inclusive group are two subgroups: the first is made up of small glands (21 in number) whose average length is 5.1 centimeters, and whose average width (at superior pole) is 3 centimeters (Fig. 9, A¹); the second is made up of glands with average length and width of 6.6 centimeters and 3.4 centimeters, respectively (Fig. 9, A²).

In the second major group (24 glands or 31.5 per cent of the total) the gland is not constricted below but maintains a uniform width throughout its length, with superior and inferior poles gently rounded. Here, again, subdivision on the basis of size can be made: a larger lot (13 specimens) with average length of 5.3 centimeters and an average width of 3.6 centimeters (Fig. 9, B¹); a smaller lot of bulkier glands, averaging 6.5 centimeters in length and 3.5 centimeters in width (Fig. 9, B²).

In the third of the main groups (6 specimens) the glands have the form of an inverted letter L (Fig. 9, C); they are almost as broad at their superior extremity as they are long. The average length of these is 5.7 centimeters, while the average width is 4.7 centimeters. The transverse portion of the L, represented by the superior portion of the gland, is made up of glandular tissue which lies along the superior border of the main parotid duct (in 1 instance reaching a length of 5.4 cm.). In all but 2 instances, this glandular tissue was associated with the superficial lobe of the gland. In the 2 exceptions, the tissue was on the same plane as the deep lobe and appeared to be part of it.

In the fourth, and last, category (6 specimens) all of the glands are large, with an average length of 6.7 centimeters, and an average width of 3.7 centimeters. The glands are roughly triangular in outline, but the broad base of the gland forms the inferior pole of the gland; the superior pole then being represented by the rather sharp apex of the gland (Fig. 9, D).

Accessory glandular masses are fairly common: 16 small nodules of tissue occurred in 15 of the 76 cases (19.7 per cent). They are invariably situated superior to the main parotid duct; sometimes partially overlapping it (Fig. 6). Although an accessory gland may be located anywhere between the anterior border of the main gland and the anterior border of the masseter muscle, in the majority of instances they are found along the proximal one-half of the duct. In length the accessory glands vary from 1.0 to 2.3 centimeters (average 1.4 cm.). In width, from 0.5 to 0.8 centimeter (average, 0.7 cm.). The long axis always corresponds to that of the main duct into which

the accessory element empties by a very short, slender duct.

Regarding the main duct of the parotid gland, it may be said that if it drains the upper portion of the gland, its course will be transverse across the masseter muscle (Fig. 1). Of the glands studied the duct pursued this course in 42 specimens, a fact which means that in these cases it was in early close association with the nerve (Fig. 1). When the duct drains the central or the lower portion of the gland, it tends to pass obliquely to the mouth (Fig. 4). Such a course was found in 32 cases. In 3 specimens "double" ducts occurred (Fig. 6). One component drained the superior portion of the gland and passed transversely with an inferior component drained the lower glandular tissue and coursed obliquely upward. A connection occurred between the two elements 1.5 to 2 centimeters beyond the anterior border of the gland.

CONCLUSIONS

So intimate is the relation of the facial nerve to the parotid gland that the scheme of nerve ramification and intercommunication can be most satisfactorily presented on such basis. In fact, the pattern of anastomosis seems to be governed by the shape and position of the deep lobe of the gland, and by the presence of an isthmus of tissue between the latter and the larger superficial portion.

Although the parotid is subject to considerable variation in size and form, it is invariably bilobed. The small deep lobe overlies the condyloid and coronoid processes of the mandibular ramus; it is likely to be ovoid in outline. The large, superficial, lobe, which conceals the lesser lobe, is usually triangular in outline, with the narrow, bluntly apical, portion more frequently directed downward than upward.

Now as the trunk of the facial nerve comes toward the surface, through the space bounded by the mastoid process of the temporal bone and the condyloid process of the mandible, it insinuates itself between the lobes of the parotid gland, in close relation to the isthmus. Thereupon it divides quickly, the divisions appearing as the divergent arms of the letter Y: one division ascends obliquely toward the temporal region while the other descends obliquely into the cervical region. Both of these divisions, and the proximal portions of the branches, are usually covered by the superficial lobe of the parotid; the divisions skirt the corresponding margins of the isthmus, and usually anastomose distally to surround and clasp it. Whether the divisions continue independently or, by conjunction, are circumferential to the isthmus,

they tend to converge as they proceed forward—slightly in the first instance strikingly in the second. In those cases in which the temporal division joins the cervical (76 per cent of specimens) the fusion occurs in such a way that the buccal branch appears to be the continuation of the confluent portions. The buccal branch is somewhat superior to the main trunk of the nerve (by a finger's breadth or less commonly), and even when the superficial lobe of the gland is prolonged forward this branch is likely to be exposed just beyond the parotid tip. It regularly overlies the parotid duct.

When the divisions remain separate the branches of the temporal portion spread out like the spokes of a quadrant of a wheel: those of the cervical portion on the contrary leave the division as if they were twigs derived from one side of a branch—the division itself continuing still a prominent branch, into the neck. When on the contrary, the divisions anastomose, the temporal, zygomatic, buccal and some of the mandibular branches, quit the loop centripetally in series—the lowermost mandibular branch at least, appearing to be a branch of the descending cervical division, not as a derivative of the loop. Just as there exist variations in the brachial or in the lumbosacral plexus of nerves, here also there are aberrancies in pattern of cords and nerves. In about 65 per cent of the cases in which anastomoses occur (76 per cent of the total number) the branches originating from the anastomotic loop are temporal, zygomatic and buccal; in the remaining 11 per cent some mandibular branches are included. This means that in the cranial two-thirds or three-fourths of the entire parotid zone the related nervous elements are likely to be involved in a plexiform scheme. In most instances the forming elements of the plexus are largely extraglandular.

Secondary anastomotic loops are fairly common, and may be either proximally or distally placed. In rare instances the space enclosed by anastomosis of the two regular divisions (temporal, cervical) of the facial trunk, may be bisected by a third division: this transverse supernumerary division would seem to be principally buccal, since it reaches the distal (anterior) margin of the loop at the customary point of origin of the nerves destined for the rima oris.

From this anatomical study certain features of a practical significance are made evident, these may be considered in the order in which they would affect the mode of surgical exposure. The parotid fascia should be opened posteriorly and reflected forward from a preauricular incision in order to expose the anterosuperior or apical por-

tion of the parotid gland. Since the gland usually possesses the outline of an inverted triangle, with the base represented by the part of the superficial lobe which coincides with the line of the zygomatic arch, exposure of the gland along its superior margin will lead the operator to its tip. When the apex has, by this maneuver been uncovered the parotid duct and the associated buccal branches of the facial nerve can be readily identified, since the duct either extends forward from the apex or lies just inferior to it. Next, employing the buccal ramus as a guide to the more proximal position of the large temporal division of the nerve, or of the point of anastomosis of the latter with the smaller cervical division, the radially directed nerves can be safely exposed in serial succession backward by progressively lifting the margin of the gland. In this process the isthmus, which connects the superficial and deep lobes, will serve as a pedicle and as a core round which the two divisions course. By tracing the large upper division dorsalward toward the ramus of the mandible, the operator will be guided to the main trunk of the facial nerve. Therefrom the small lower division can be followed along the inferior margin of the isthmus and downward toward or into the neck. Having thus reached an area where the divisions and rami are strongest and their patterns of branching least complex, glandular tissue may be excised with minimal danger to the facial nerve.

Because the parotid gland is sometimes small or is so formed as to be constricted cranially, more than the regular fraction of the main divisions may be apparent beyond the periphery of the parotid. Obviously when such an arrangement obtains special care must be exercised if the branches are to be spared trauma or transection.

SUMMARY

A study of the facial nerve, especially in relation to the parotid gland, was conducted in 100 carefully prepared dissections of adults.

From the data collected (in the form of artist's drawings and authors' sketches) the bilobed nature of the parotid gland was definitely established as was also the regular position of the facial nerve between the two glandular portions, namely, superficial larger part and deep smaller portion.

From examination of the collected records of facial nerve ramification it was found that all could be conveniently and graphically catalogued as belonging to one of a total of eight types, in which those with anastomoses between major divisions or between branches of either of the latter outnumbered the nonanastomotic types in

the proportion of 3:1. It was also learned that in the specimens where anastomosis took place, the loop thus formed surrounded the isthmus of the parotid gland.

The types were illustrated by diagrammatic drawings from actual specimens and detailed drawings, from similar source were secured to portray the relationship between the nerve's divisions and branches to the lobes of the parotid gland.

On the basis of the morphological conclusions, some opinions are expressed on importance of the observed facts to procedure in extirpation of the gland. These deal with the manner of reflecting the superficial parotid lobe, the resultant exposure of all larger nervous elements, the existence of an area where nerves are concentrated the service

ability of identifying the common relationship of the buccal component to the parotid duct.

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CAUSALGIA

FRANK H MAYFIELD M.D. F.A.C.S., Major M.C., A.U.S., Cincinnati Ohio and

JOHN W DEVINE, M.D., F.A.C.S. Captain M.C., A.U.S., Lynchburg Virginia

THE term causalgia was used in 1865 by Mitchell Morehouse and Keen to describe a bizarre syndrome resulting from injuries to peripheral nerves. Its cardinal features are the subjective complaint of burning pain in association with trophic and vasomotor changes in the injured extremity. The pathology and pathogenesis of causalgia are unknown. Indeed there is some confusion as to what constitutes a case of this condition. Some writers (1, 2, 4) believe that causalgia is atrophy, painful osteoporosis, and other so called "minor causalgias," and indeed painful phantom limb are different clinical manifestations of the same underlying disorder. The similarity however is remote and we are of the opinion that causalgia varies sufficiently in severity to be considered a clinical entity.

In this paper we will present the data from 15 cases, in which the symptoms and objective findings were of sufficient severity to compare with those described by the original authors. These cases have been studied to correlate subjective and trophic changes with blood flow in the part. Blood flow was determined by means of the oscilometer, skin temperature readings, and at times the histamine flare test. In addition all patients have had psychiatric examination because of the belief by some that predisposing constitutional psychic factors play an etiologic rôle. The effect of interruption of the sympathetic chain with procaine block and by surgery, and the effect of hyperthermia have been observed.

These studies suggest that the pain of causalgia does not result from alteration in the blood flow. For some patients are found in whom the injured extremity is in a state of vasodilatation while others show vasoconstriction. The trophic changes and the response to heat and cold vary considerably with the blood flow. The severity of trophic changes increases with prolongation of symptoms.

MATERIAL

The 15 cases were encountered in a group of 100 peripheral nerve injuries (2¹). The median nerve (6), ulnar (5), radial (3), peroneal (3), and sciatic (2). The patients were treated by the following: 1. Physical therapy, 2. Procaine block, 3. Sympathectomy, 4. Amputation, 5. Prosthetic, 6. Psychological, 7. Combination of two or more.

was involved in 7 cases, the median and ulnar in 1, the brachial plexus (median and lateral cords) in 1. The sciatic nerve was involved in 6 cases. In each instance the wound was of a penetrating type due to bullet or shell fragment and was proximal to the elbow or knee. Two patients were officers, 13 were enlisted men. Their ages ranged from 23 to 33 years. The wound became infected in 2 cases. Sizeable foreign bodies were retained at the level of the injury in 3 cases. The nerve lesion was incomplete in each instance. This syndrome has not been seen in any individual in whom the nerve was completely divided. No patients have had any major vascular injuries. Three of the patients had also suffered a concomitant fracture of the femur.

SYMPTOMS AND SIGNS

Mitchell Morehouse and Keen noted that the onset of burning pain was usually late, at times being delayed as much as 1 to 2 months. They observed that pain was always present in the distal part of an extremity, usually in the palm or in the dorsum of the foot, and not confined to the autonomous zone of the injured nerve. They commented that certain patients had warm skin and others cold but placed greater stress on the glossy, shining skin and loss of hair, etc., and considered that these changes would appear in all cases of long duration.

In 9 of the 15 cases here reported the burning pain was present from the moment of impact. In 3 others it appeared within 24 hours. In 3 it was delayed as long as 3 weeks. The pain was of intense burning character and varied in intensity with emotional stimuli such as anxiety, anger, or fear. Noises such as the scraping of a chair, the tearing of paper, loud music, or breaking glass caused intense suffering. Lighting the room without warning would often provoke a severe paroxysm of pain.

Eleven of the 15 patients obtained some relief from the application of moisture. It was Mitchell's (6) opinion that moisture was the factor which afforded comfort rather than the temperature. Nine of our patients preferred cold water, 2 obtained some relief from warm water, and in 3 cases the effect of moisture was not significant. Throughout

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MATERIAL

The 15 cases were encountered in a group of 737 peripheral nerve injuries (2%). The median nerve

From the Neurosurgical Section, Percy Jones General and Convalescent Hospital, Battle Creek, Michigan. Read before the annual meeting of the Association for Research in Nervous and Mental Diseases.

was involved in 7 cases, the median and ulnar in 1, the brachial plexus (median and lateral cords) in 1. The sciatic nerve was involved in 6 cases. In each instance the wound was of a penetrating type due to bullet or shell fragment, and was proximal to the elbow or knee. Two patients were officers, 13 were enlisted men. Their ages ranged from 23 to 33 years. The wound became infected in 2 cases. Sizeable foreign bodies were retained at the level of the injury in 3 cases. The nerve lesion was incomplete in each instance. This syndrome has not been seen in any individual in whom the nerve was completely divided. No patients have had any major vascular injuries. Three of the patients had also suffered a concomitant fracture of the femur.

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In 9 of the 15 cases here reported, the burning pain was present from the moment of impact. In 3 others it appeared within 24 hours. In 3 it was delayed as long as 3 weeks. The pain was of intense burning character and varied in intensity with emotional stimuli such as anxiety, anger or fear. Noises, such as the scraping of a chair, the tearing of paper, loud music, or breaking glass, caused intense suffering. Lighting the room without warning would often provoke a severe paroxysm of pain.

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TABLE I.—SUMMARY OF CASES

Case Age	Injury	Duration	Onset	Relief from measures	Blood flow	Treatment	Result
1. F.H.M. 20	Bullet, left thigh	3 mo	Immediate	Warm	Reduced	Sympathectomy lumbar L3-4	Relief
W.W.D. 24	Shell fragment, left thigh	3 mo	Immediate	Cold	Increased	Sympathectomy lumbar L3-4	Relief
3. L.C.K. 3	Bullet, right arm	mo	Immediate	None	Increased	Sympathectomy dorsal, 8th, 9th and 10th	Relief
4. J.G. 28	Bullet, right shoulder	3 1/2 mo	Immediate	None	Increased	Temporary relief after procaine block	Relief
5. A.B. 3	Bullet right arm	7 mo	24 hours	None	Increased	Temporary relief after procaine block	Relief
6. J.U. 23	Shell fragment left thigh	3 1/2 mo	24 hours	Warm	Reduced	Fever therapy 3 weeks	Relief
7. G.T. 27	Bullet, left thigh fractured femur	mo	3 weeks	Cold	Increased	Sympathectomy lumbar L3-4	Relief
8. G.L. 27	Shell fragment left thigh; fractured femur	mo	3 weeks	Cold	Increased	Sympathectomy lumbar, L3-4	Relief
9. D.C. 3	Shell fragment left thigh; fractured femur	8 mo	hours	Cold	Increased	Sympathectomy lumbar L3-4	Relief
10. K.S. 20	Shell fragment left arm	mo	Immediate	Cold	Increased	Sympathectomy lumbar L3-4	Relief
J.L. 4	Shell fragment left arm	mo	Immediate	Cold	—	Sympathectomy dorsal, preganglionic	Relief
11. B.G.	Bullet, right arm	24 hr	Immediate	Cold	—	Sympathectomy dorsal, preganglionic	Relief
12. K.M. 20	Bullet, left arm	mo	Immediate	Warm	Reduced	Sympathectomy dorsal, preganglionic	Relief
14. R.S. 26	Bullet, left ankle	mo	3 weeks	Cold	Increased	Sympathectomy dorsal, preganglionic	Relief
15. R.B. 24	Shell fragment right arm	mo.	Immediate	Cold	Increased	Sympathectomy dorsal, preganglionic	Relief

*Prior to neurolysis, warm water afforded relief; after neurolysis cold water afforded relief.

†Spontaneous recovery but hyperaesthesia to cold.

‡Wound high, right thigh. Removal lumbar ganglia 3 & 4 produced no relief. Removal lumbar ganglia 2 followed by caustic relief.

the course of the disease, in our cases, the patients demands for cold or hot water did not change except in 1 instance. In Case 2 intense burning pain developed from a partial lesion of the left sciatic nerve above the knee. For 3 1/2 months after injury at which time neurolysis was done, warm water had afforded some relief. Thereafter warm water was painful but cold water caused marked lessening of pain and the patient kept the foot immersed in iced water until it was necessary to withdraw it, to prevent vascular damage.

Three patients kept their hands constantly covered with a wet cloth. Another (Case 11) maintained a basin of water at his bedside (Fig 1) for this purpose. Without exception, the patients exercised great care to prevent the part being touched, particularly by rough objects. One (Case 4) kept the hand protected constantly in dry flannel (Fig 2). Most patients would go to what appeared to be absurd extremes to prevent motion of the part. Some would grasp the painful

extremity just proximal to the wrist or ankle with the normal hand, and hold this position for hours. The facial expression usually reflected intense suffering (Fig 3).

In the more severe cases the patients were poorly nourished due to low food intake, and were irritable and shut in, showing no interest in family or friends even though they had been overseas for many months. They preferred to be alone in a darkened room. They were unduly critical of attendants. The case histories in most instances revealed items of information such as these, which suggested that the disorder might be entirely psychogenic in character. Mitchell stated that the word "hysterical" seemed to describe the state best.

The motor and sensory loss was difficult to determine for usually the patient refused to move the part or permit it to be touched. In addition, there was usually marked stiffness of the joints, due to disuse.



Fig. 1 Case 11. Photograph shows method devised by patient to keep hand constantly wet.

The trophic changes were generally of two types. In the first type of which we have had 3 cases the skin was cold, thin and glistening, the superficial layers were denuded and sweating profuse. With this there was loss of hair, tapering of the digits and a tendency of the nails to curl. Oscillometric examinations showed marked vasoconstriction as compared to the opposite extremity and the skin temperature was from 2 to 6 degrees lower than in the normal limb. The pain was lessened by application of warm water. One case of this type (Case 1) developed intercurrent malaria (*Plasmodium vivax*). During elevation of temperature he was completely free of pain. This was true with each of the three chills. The pain returned when the malaria was controlled. An additional case (Case 7) was given three bouts of artificial fever therapy, each of 3 hours duration with a tem-

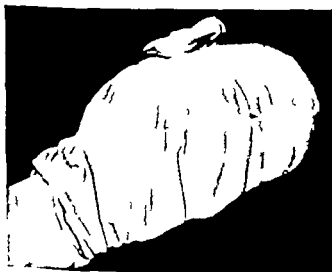


Fig. 2. Makeshift protective covering of dry flannel constantly worn.



Fig. 3 Case 5. Photograph showing facial expression and the patient immobilizing the painful member by holding it with the other hand.

perature of 104 degrees. Pain disappeared immediately with the elevation of temperature and returned in mild form with the fall of temperature after the first two bouts. There was no return of pain after the third.

In the second and more frequent type (9 cases) the skin of the painful part was warmer than that of its opposite member and the hair long and coarse (Fig. 4). The skin was relatively dry and at times actually scaly. In three instances the skin was smooth but was not comparable to the glossy skin of those in vasoconstriction. These patients experienced relief from cold water and the pain was exaggerated by application of heat, either moist or dry. One patient (Case 8) who was placed in a fever cabinet experienced such severe pain that he had to be removed within less than 1 hour. Oscillometric examination on these patients, when it could be done, showed the involved extremity in vasodilatation. The skin temperature of the painful part was from 2 to 5 degrees warmer.



Fig. 4 Case 4. Excessive hair growth is present in causalgic limb.

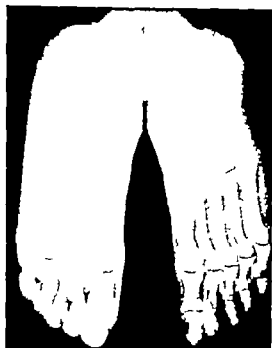


Fig. 5. Spotty osteoporosis of the small bones of painful right foot

The severity of the trophic changes increased with the duration of symptoms, yet the types seemed unchanged.

In 3 cases, oscillographic and skin temperature studies were not carried out

OSTEOPOROSIS

In 9 cases the extremities were examined roentgenographically for evidence of osteoporosis. As has been demonstrated by Miller and de Takats, there was spotty osteoporosis of the small bones of the hands and feet in each case with vasodilatation (Fig 5). If the duration of the illness was long extending more than 3 months, the demineralization tended to become generalized. The 3 patients who showed vasoconstriction also showed demineralization of the painful part, but it was not spotty.

TREATMENT

Success has been reported with many forms of treatment in causalgia. Mitchell, Morehouse and Keen used leeches. Direct surgical attack on the nerve trunk above, below and at the level of injury is reported to relieve the syndrome at times. Varying degrees of success have been reported with drugs and physiotherapy. Interruption of the sympathetic chain has consistently been the most efficacious procedure.

Of our cases, one was relieved by fever therapy and two recovered spontaneously. The remainder

were treated by interruption of the sympathetic chain. Every patient had repeated procaine block of the appropriate chain. The least number of injections given to one patient was 3 and some patients have had as many as 8. The relief following injection was dramatic. It was instantaneous and absolute, and usually was maintained for intervals of from 1 to 3 hours, after which the pain returned reaching its maximum intensity within a short while. We have not been able to provide any lasting benefit by this procedure, and have subsequently interrupted the sympathetic chain with surgery. Despite this brief period of complete relief the patient almost invariably objected to repeating the procedure because of fear of being stuck.

Cervicodorsal sympathectomy was done on 1 case in which the arm was involved, the stellate and second dorsal ganglion being removed. Six cases with arm involvement were treated by preganglionic ramisection.

In 5 of the 6 cases in which the leg was involved, the 2d, 3d and 4th lumbar ganglia were removed. Four were entirely free of pain upon awakening from the anesthetic and have remained well to this date. In 1 case (Case 8) removal of the 3d and 4th lumbar ganglia only was done at an initial operation because of technical difficulties, and pain persisted. Subsequently the 1st and 2d lumbar ganglia were removed, with complete relief.

Neurolysis was done in 5 cases, and periaxillary sympathectomy at the level of the injury in 3. The pain was not influenced by these procedures.

It was impressive to observe the remarkable change in the patients' attitude and behavior following relief from pain. Without exception they became pleasant, co-operative, and happy, and showed interest in their families and friends. In several instances the recovery of function after sympathectomy was rapid, suggesting that reflex paralysis was present. In many the nerve injury was mild and the ultimate recovery after sympathectomy was good. Each patient in this series, however, was left with a rather marked hyperesthesia in the autonomous zone of the involved nerve. During the period of pain the patient would not move the part and the joints stiffened rapidly. In the majority of instances this was the chief residual disability. The stiffness was more marked in those cases of long duration.

PSYCHIATRIC ANALYSIS

Each patient of this group was submitted to a psychiatrist for examination after being relieved of the pain and each one was classified as a nor-

mal individual with a stable personality. Six patients were returned to duty. 4 were discharged for residual disability of the injured nerve but without pain. Five are still under observation.

ANALYSIS OF STUDY

The material on which this paper is based is not sufficient to permit final conclusions. It is possible that additional observations will show that the trophic changes are not always consistent with the alterations in blood flow as we have observed. It is also possible that the blood flow in a causalgic limb may vary from time to time, but this has not been observed.

The permanent relief of pain which accompanies interruption of the sympathetic chain suggests that the mechanism of relief is by interruption of an afferent pain pathway. The relief of pain which accompanies the application of warm or cold moisture distal to the injury and the relief accompanying hyperthermia however is not consistent with this argument and is not understood.

The personality changes always present during the painful stages are secondary to the pain. There is no evidence in our cases that there is a predisposing constitutional psychic factor.

SUMMARY AND CONCLUSIONS

In a study of 15 cases of causalgia the following observations were made:

1. Burning pain is a constant complaint and is usually immediate in onset.
2. The median or sciatic nerve was involved in each instance and the lesion was incomplete.
3. Certain patients showed vasoconstriction in the causalgic limb others showed vasodilatation.
4. The trophic changes and response to warm or cold moisture and to hyperthermia varied depending upon the blood flow.

5. Twelve patients were relieved by sympathectomy of the involved limb. 1 was cured by artificial fever therapy and 2 recovered spontaneously.

6. Further observation as to the value of fever therapy will be made.

7. Direct surgical attack (neurolysis) upon the injured nerve which was performed on 5 cases and penarterial sympathectomy at the level of injury performed in 3 have not been of benefit.

8. Procaine block of the sympathetic chain affords complete relief temporarily and should be repeated 2 to 3 times, although no case in this series has had any lasting benefit from this procedure.

9. Sympathectomy (preganglionic) gave immediate and lasting relief to 12 patients.

10. The site of injury must be included in the sympathectomy.

11. Sympathectomy should be done early to prevent stiffness of joints due to disuse.

12. The personality changes always present during the painful stages are secondary to the pain. There is no evidence in our cases that there is a predisposing constitutional psychic factor in causalgia.

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A SAFE SIMPLE AND EFFICIENT METHOD OF INTESTINAL ANASTOMOSIS

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NO one single method solves the problem of how best to do an intestinal anastomosis. Many fine methods, some extremely ingenious, have been described and all have their good points and probably all are equally efficient in hands trained to use them. Most require specially designed instruments in addition to special skill in the use of these instruments.

However it is one thing for an expert surgeon thoroughly trained and adequately equipped to elect to do a resection and anastomosis, and for an unskilled surgeon who operates only occasionally to be suddenly confronted with the necessity of doing one as an emergency. Many emergencies require resection and many such cases are handled by surgeons neither trained nor equipped to do a resection. It seemed to me that if a method of anastomosis could be worked out whereby only the ordinary instruments found on the usual hospital tray were necessary many more surgeons might be able to make use of it. The method to be described was therefore devised. The operation can be readily carried out with the use of only standard hospital instruments. The method is almost fool-proof even for those of little training if the steps are carefully carried out. Recently Stevenson and Totten have published descriptions of two other methods designed probably with the same thought in mind careful study of these articles is recommended.

TECHNIQUE

Instruments Either long Kocher or straight Ochsner hemostats are used. I use two long Ochsner hemostats with the end teeth filed smooth (Fig. 2 insert) although this is not essential. A small rubber tubing screw clamp is used to hold the forceps together (Fig. 6 insert, A) while the anastomosis is completed. This clamp is found in every hospital intravenous set and does not have to be of the design shown here any small tubing clamp will do. A few curved Kelly or mosquito hemostats are useful. No. 0 chromic catgut sutures on straight atraumatic intestinal needles are used. For the outside or last row of sutures, a long

thread with an atraumatic needle on each end is useful but not essential.

Procedure. Step 1. The segment to be removed is determined, and the lines of section are chosen. At these two points a blunt hemostat is pushed through the mesentery and a hole is made which is enlarged toward the diseased segment (Fig. 1). Enough mesentery is denuded so that the area for anastomosis will be mesentery free. The hemostats (crushing) are so applied that the mesenteric border comes to the center of the crushed area, not at one end of it. The hemostat therefore is applied at right angles to the mesentery (Fig. 2) not parallel to it. Totten is, I believe the first to describe this step and deserves credit for so doing, but I have been using it for some time. Two heavy straight hemostats are also placed on the diseased segment, which is then cut away with a cautery as usual. We now have the situation as shown in Figure 2.

Step 2. With a straight intestinal needle, a through-and-through suture is placed across the end of each bowel end (Fig. 3). This suture passes through and through from side to side, just as closely below the hemostat as possible but does not pass over it. It is most convenient for the operator holding the hemostat in his left hand, to start the suture at the end of the hemostat and sew toward the handles. The first and last bites must be taken in the very edge of the bowel itself. Each bowel end is so treated.

Step 3. Each hemostat is taken off (Fig. 4) and carefully reapplied (Fig. 5) so that its tip end is not quite level with the edge of the bowel wall (Fig. 5). The hemostat is reapplied in the original crushed area and its tip must catch the end of this first suture which is cut short after being caught in the end of the hemostat (Figs. 5, 6). The reapplication of the hemostat is an important step.

Step 4. The hemostat blades are laid side by side and held together with the screw clamp (Fig. 6). To avoid having any space between the distal ends of the hemostats, a small piece of metal bent on one end (Fig. 6 insert, B) is used to pry the handles apart. A sterile tongue blade, always available, will serve the same purpose. If the hemostat blades are long enough the screw clamp

Read before the Texas Surgical Society, Galveston, Texas, October 3, 1944.

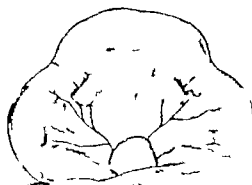


Fig. 1

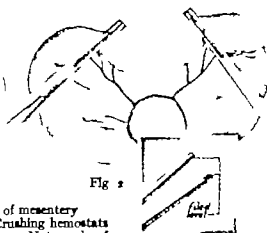


Fig. 2

Fig. 1. Area of anastomosis denuded of mesentery.
Fig. 2. Diseased portion removed. Crushing hemostats are placed at right angles to mesentery. Note ends of hemostat projecting slightly beyond bowel walls. The insert shows ends of Ochsner hemostat filed smooth.

can be applied distal to the lock, thus making possible exact approximation of the blades. Like Totten I had had a special holding device prepared but this simple screw clamp is far superior. The operation can be done without the use of the screw clamp but with it the procedure is materially simplified.

Step 5 Suturing is now begun. Interrupted mattress sutures are used, the first being placed so as to cover the ends of the hemostat. Unless the hemostat has been pulled back and reapplied as described in Step 3 the ends would have to remain protruding. These mattress sutures are placed about halfway up the clamps (Fig. 6) and tied (Fig. 7).

Step 6 At this point the hemostat is rotated 180 degrees, and half of the posterior side is likewise treated (Fig. 8).

Step 7 The hemostat is rotated back to its original position, the screw clamp is removed both blades of the hemostat are loosened and pulled back enough so their ends are only halfway across the crushed area and just under the last tied stitch. They are then reapplied and the screw clamp again put on (Fig. 9).

Step 8 The anterior row of sutures is now completed the hemostat rotated again and the posterior row also completed. As the last mattress suture is made ready to tie the clamp and hemostat are loosened and pulled out completely (Fig. 10).

Step 9 With a long thread of No. 0 chromic and anatraumatic needle on each end a running suture is placed completely around the anastomosis. This row of sutures is started at the point where the short ends of the first sutures are located half of the suture material being used for the anterior half for the posterior layer (Fig. 11). This is tied

Step 10 The original through and through sutures across both bowel ends are now grasped by the long ends, which were left uncut when inserted and are pulled out. Until these sutures are pulled out no spillage from either bowel end could occur accidentally even if the bowel end should pull out of the holding forceps as occasionally occurs.

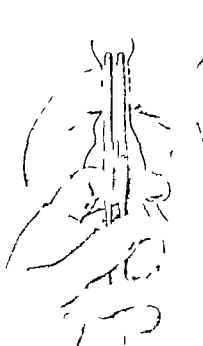


Fig. 3

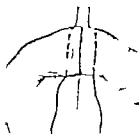


Fig. 4



Fig. 5

Fig. 3. Through and through sutures in place across each bowel end.

Fig. 4. Hemostat momentarily removed.

Fig. 5. Reapplication of hemostat. Note that ends of instrument do not go quite to extreme edge of bowel wall, and that short end of suture is caught in blades at tip.

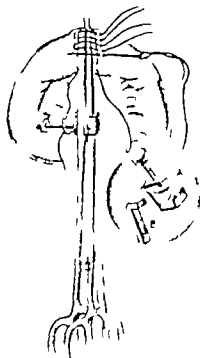


Fig. 6

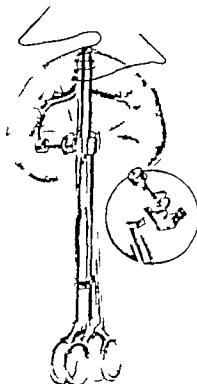


Fig. 6a.



Fig. 7



Fig. 7a.

Figs 6a to 7a, inclusive, show method of anastomosis by using continuous suture for the first layer mattress sutures for the second

Fig. 6 Placing of anterior sutures. The first stitch

should cover ends of clamps. Not a screw clamp is placed. The clamp locks, and use of edge between handles eliminates space between clamp blades. Insert shows clamp and edge

Fig. 7 First half of anterior row completed.

Sutures must be placed deeply enough to catch the submucous layer. Failure to do this may and often does result in leakage. When the needle point is placed deeply enough as the suture is started the bit of tissue over it is white and blanched as upward pressure is made. If one can see the needle point all the time it is not deep enough.

Some prefer to use a running stitch as the first row instead of the interrupted mattress sutures. This is very easy to do with this technique and is shown in Figures 6a, 7a, 8a, 8b, 9a, 10a, and is

somewhat faster. I would call attention at this point however to the very great importance of placing the interrupted mattress sutures first. By so doing the danger of any pursestring effect is obviated. When the running suture is used as the first row the pursestring tendency which develops as the suture is drawn taut is difficult to prevent. The method recommended offers considerable protection against this tendency to contract and reduce the diameter of the anastomosis.

Several steps of prime importance are worthy of mention

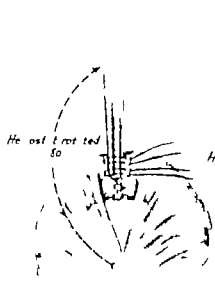


Fig. 8.

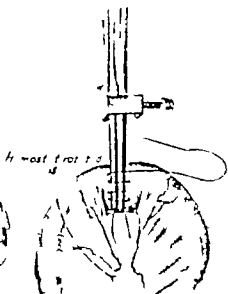


Fig. 9a.



Fig. 9b.

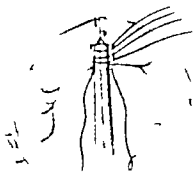


Fig. 9c.

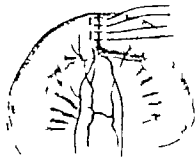


Fig. 9d.

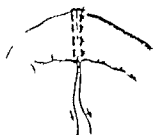


Fig. 10.



Fig. 10a.



Fig. 11.

Fig. 8 Hemostat is rotated first half of posterior row of sutures is placed and tied.

Fig. 9 Hemostat has been rotated back to original position loosened pulled back so that ends are just under last tied anterior stitch, reappled and rest of anterior row of sutures is placed and tied. Hemostat is then rotated again

to position as in Figure 8 and rest of posterior row is completed, after which hemostat is withdrawn completely

Fig. 10 First row of sutures is completed. Note the two original through-and-through sutures still in place. They can be removed now or after the running stitch is placed

Fig. 11 Placing of the last row of sutures, continuous.

1 The hemostats are so applied that the mesentery comes to the middle of the hemostat

2 The portion of bowel to be used in the anastomosis must be denuded of mesentery

3 A through and through suture in each bowel end, if used as described absolutely prevents any accidental spill at any stage of the operation even if the bowel end drops out of the clamp

4. The method of loosening and reapplying the clamps permits more accurate placing of the sutures, with the turning in of the minimum amount of bowel end. If a very thin bladed hemostat had the rigidity of the heavier ones, this step might be avoided.

5. It is important that every stitch must catch up the submucosa if it is to have any holding power.

6. The use of interrupted mattress sutures as the first layer is urged because they prevent the

pursestring effect accompanying the use of a continuous stitch as a first layer.

7. The method described is simple and safe. It is not aseptic, only relatively so. It requires no special instruments or training and by the use of a simple screw clamp the services of an experienced assistant are not essential.

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TRANSVERSE UPPER ABDOMINAL INCISIONS

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THE transverse upper abdominal incision has many advantages over the longitudinal rectus muscle splitting incision for upper abdominal surgery. These advantages are (1) the blood supply of the abdominal wall is interfered with but little (2) the nerve supply of the abdominal wall is not damaged (3) the wound tends to come together naturally (4) postoperative distention if present puts much less strain upon the wound than when a longitudinal incision is used (5) patients resist deep breathing much less and thus the incidence of postoperative pulmonary atelectasis is lessened (6) it affords better exposure of the upper abdomen with less necessity for the packing away of the small bowel (7) wound disruption is less frequent and more readily repaired when it does occur (8) the danger of postoperative hernia is less (9) patients may be allowed out of bed very early because the sitting or upright position decreases rather than increases the strain on the wound.

The transverse upper abdominal incision also has certain disadvantages (1) it is more time consuming (2) in some cases, if an appendectomy is to be combined with an upper abdominal procedure

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it may be difficult or occasionally impossible to accomplish this step through the upper abdominal incision (3) in some cases, in the presence of a narrow subcostal angle the exposure is no better than it is through a longitudinal incision (4) in cases of total gastrectomy while some operators believe that the high left rectus muscle splitting incision gives better exposure, others do not concur in this opinion (5) cutting across the rectus muscle transversely appears to be physiologically unsound and it is because of the fear of possible irreparable damage which may follow that many surgeons prefer not to use this incision.

In order to learn what actually happens to the cut ends of the muscle we made a study of the results in dogs of cutting the rectus muscle transversely and resuturing the fascia without suturing the muscle. After a 2 month interval we reopened the wound and found the muscle densely adherent to itself at the cut ends and also to the overlying and underlying sheath which in effect, gives an additional *inscriptio tendinea* in the muscle.

A study of microscopic sections revealed that the cut ends of the muscle showed the same kind of healing as was found after the use of the muscle fascia suture as done by Koontz, and by Rosenblatt and Cooksey namely a connective tissue union occurred between the two cut ends of the

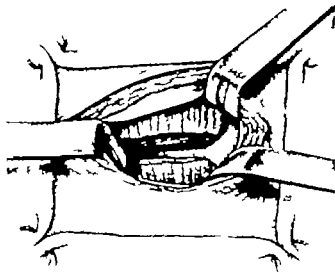


Fig. 1. Transverse incision of rectus muscle of dog

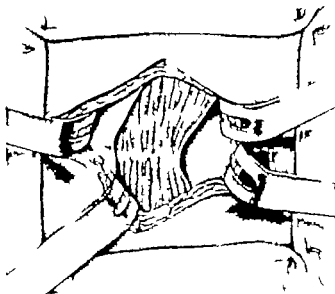


Fig. 2. Healing 2 months later



Fig. 3.

Fig. 3. Type of union at cut edge of muscle.



Fig. 4.

Fig. 4. Higher power photomicrograph showing connective tissue cells in and around the muscle interlaced with fibrous tissue bridging the muscle gap.

muscle. White fibrous connective tissue cells were always present in the muscle because the muscle bundle was surrounded by a sheaf of white fibrous connective tissue and each muscle fiber was surrounded in a like manner and the entire muscle or group of muscle bundles was also held together by connective tissue cells. These elements from both sides join and make a very firm union due to the fact that the connective tissue elements are anchored like tentacles in and around the muscle fibers and bundles.

A study of the accompanying photomicrographs will demonstrate the presence of the endomysium, perimysium, and myomysium (the connective tissue cells around the muscle) and the hundreds of interlacing strands of connective tissue which in this manner anchor the cut ends of the muscle

together. In general, from our study we are convinced that very firm and satisfactory healing of the cut muscle occurs and that the union thus formed is fascial in character and equivalent to an additional inscriptio tendinea.

In summary, we believe that for many cases the advantages of the transverse upper abdominal incision outweigh its disadvantages. The point of view that cutting across the rectus muscle may lead to difficulties in healing is only psychological, as is evidenced by the type of union obtained in this study.

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PRIMARY TUMORS OF THE LIVER

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THE paucity of recent literature on the subject of primary tumors of the liver and the futility with which such tumors are usually regarded are indicative of the need for pointing out favorable aspects in order that patients who would benefit by surgery will not be denied early adequate treatment.

An outline of primary tumors of the liver excluding tumor like hyperplastic nodules and secondary tumors, will serve as a basis for discussion of diagnosis and treatment

TRUE PRIMARY TUMORS

1. Hepatomas
 - a. Liver cell adenomas
 - b. Liver cell carcinomas with or without cirrhosis
2. Cholangiomas
 - a. Adenomas of intrahepatic bile ducts, solid or cystic
 - b. Carcinomas
3. Cholangiohepatomas of both liver cell and duct elements
4. Tumors primary in the liver but not of specific hepatic elements (vascular fibroses, adrenal rests, etc.)

Adenoma is limited to benign encapsulated tumors of glandular origin and hence excludes all those with blood vessel or regional invasion and those with metastasis. This eliminates such paradoxical terms as malignant adenomas.

Some authors (Benson and Penberthy) would separate the smaller slowly growing benign rests of liver cells from adenomas by calling them hamartomas. However they resemble adenomas in appearance and when large enough to be manifest they behave like adenomas clinically requiring the same kind of treatment and hence there is no practical advantage of attempting a separate classification of hamartomas.

The hyperplastic nodules of multiple foci of regeneration in cirrhotic livers do not meet the criteria of adenomas. They are without true capsules and are only surrounded by condensation of fibrous tissue of the cirrhotic process. They are not autonomous, for their physiologic secretory activity corresponds to that of the rest of the liver and through functioning duct system it is drained with that of the liver as a whole.

Adenomas of liver cells grossly are isolated, encapsulated masses of atypical cells arranged in cords with intervening blood sinusoids,¹ but with

Dr Warvi was killed in an automobile accident after receipt of this manuscript.

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no bile ducts or portal trads. The uniform large cells have eosinophilic granular cytoplasm and central nuclei, usually single but at times multiple with minimal proliferative activity and no hyperchromatism. There are no signs of peripheral nor blood vessel invasion and metastasis does not occur from these benign lesions (see Figure 1 a and b of a benign adenoma that was resected)

Carcinoma of liver cells is characterized by increased proliferative activity, resulting in smaller cells with less cytoplasm, loss of granularity, a change from eosinophilic to basophilic staining quality, and nuclear hyperchromatism accompanied by rapid proliferation by amitosis or atypical mitosis. There are no signs of secretion such as gross bile staining or microscopic plugs of inspissated bile nor is there time for calcification of necrotic portions of the tumor as there is in adenomas. Typical lesions of each class are easily recognized but the borderline types cause difficulties in determining the exact pathologic significance and therapeutic requirements.

Cholangiomas are more easily classified into benign or malignant types of either cystic or solid tumors.

Primary tumors from nonspecific elements in the liver such as vascular or stromal tumors, do not differ pathologically from similar tumors in other parts of the body and hence need no special mention.

CLINICAL DIAGNOSIS

Low incidence of primary tumors of the liver is not conducive to frequency of correct diagnosis. At the Cincinnati General Hospital there were 353,971 admissions from 1916 to 1941 inclusive. These admissions were typical of a general hospital and include minor cases as well as readmissions. A total of 73 cases were clinically diagnosed primary carcinomas of the liver on the basis of symptoms and signs as well as x ray and laboratory studies. However only 43 cases had microscopic studies, which showed the clinical diagnosis to be correct in 31 cases and incorrect in 12. This proportion of incorrect diagnoses indicates the clinical error to be 20 of the 73 cases, leaving 53 probable cases or an incidence of 0.015 per cent of total admissions as cases of primary carcinomas of the liver. With a much greater incidence in tropical countries the proportion of correct clinical diagnosis is higher (Tull Strong and Pitts)

TABLE I — FREQUENCY OF SYMPTOMS AND SIGNS IN PRIMARY CARCINOMA OF THE LIVER

Symptoms and signs	27 proved cases of C.G.I.L. Per cent	200 proved cases reported in literature Per cent	34 cases reported by Tull Per cent
Anemia	97	68	38
Weakness and weight loss	94	88	88
Palpable tumor	9	68	68
Jaundice	86	34	34
Pain	7	5	1
Fever	53	34	38
Vomiting	44	1	
Edema of legs	40	60	84
Ascites	37	46	48
Fixed diaphragm	8	30	38
Tender liver	5	7	15

Adenomas of the liver can be diagnosed clinically by symptoms and signs that are of longer duration before the patient finds it necessary to come for treatment and more localized in the right upper quadrant than carcinoma. The presence of an upper abdominal mass and a sensation of fullness or dragging is usually the first manifestation of an adenoma noted by a patient, in contrast to the distinct pain of carcinoma. Local obstructive manifestations affecting the gastrointestinal tract, bile ducts, or portal circulation, causing vague indigestion, vomiting, jaundice, or ascites are more prominent and may eventually cause death without the systemic disturbances of carcinoma and its metastases. Fever is exceptional in adenomas and present only in large ones undergoing necrosis, but is reported present in at least half of carcinomas. Cystadenomas have the signs of a cystic tumor in addition to the manifestations of a mass crowding surrounding structures and hence is more easily differentiated from malignant growths but other lesions must be considered.

Symptoms and signs of primary carcinoma of the liver are given in Table I.

The variations in the percentage of occurrence of manifestations of carcinoma of the liver in the table are indicative of the difference in the behavior of the type of carcinoma predominating in various geographical locations. The symptoms and signs of anemia, palpable tumor, jaundice, pain, and vomiting are associated with tumors of longer duration and of larger size as in our cases, while those of weakness, weight loss, fever, peripheral edema, ascites, and fixed diaphragm are present with rapidly disseminating and invasive tumors such as in Tull's cases. The manifestations in the total 500 cases represent more of an average of symptoms and signs, including those of the highly malignant ones occurring in Asiatic countries as well as those of lower malignancy reported

from Europe and America. Bile duct carcinomas of the liver tend to be more malignant with symptoms and signs of greater severity than those arising from liver cells. In our cases, 9 were of bile duct origin with an average survival of only 14 months from the onset of symptoms to death, in contrast to an average of 8 months' survival in 11 cases of carcinoma of liver cells.

Unusual symptoms and signs have been reported such as those of an acute abdominal accident when spontaneous rupture of a necrotic tumor causes intraperitoneal hemorrhage (Binkley). The pain, fever, and hematemesis from associated esophageal varices adds difficulties to diagnosis of some carcinoma cases. Adhesions about an adenoma may simulate the fixation of carcinoma and can be differentiated only by exploratory laparotomy (Farani).

Laboratory studies as a rule do not aid in differential diagnosis but are essential in determining physiologic disturbances to be corrected before operation. One exception is when a tumor is found associated with jaundice. Then the laboratory findings of acholic stools, absence of urobilinogen and direct van den Bergh differentiate obstructive jaundice suggestive of a large adenoma rather than the hepatic failure of carcinomatous involvement. An anemia must be corrected preoperatively. Prothrombin and bleeding time should be returned to normal. Low results in liver function tests (Bargen and Rankin, Cohen and Helhuis, Moranze, Moranze and Rothman) and the presence of hepatic hypoglycemia would indicate extensive liver damage due to an inoperable tumor.

Biopsy is imperative in diagnosis of liver tumors and it can best be obtained during an exploratory laparotomy, permitting inspection of the tumor for extent of involvement, invasiveness, cellularity, presence of encapsulation or of metastases. No alarming bleeding has occurred if hemostatic sutures are placed in readiness before the excision of an adequate wedge of liver tissue. Peritoneoscopy also offers some opportunity to determine operability in addition to obtaining biopsy for microscopic study (Beling). Aspiration biopsy is reported to give 73.5 per cent correct diagnoses of liver tumors at Memorial Hospital at New York. Punch biopsy has a few advocates.

Diagnostic accuracy in reported cases of resected tumors of the liver is difficult to ascertain, for from a total of 214 cases reported completely enough to tabulate the method of resection, results, and pathologic diagnosis, only 45.1 per cent gave a definite preoperative clinical diagnosis. However, most of those not stating a definite

TABLE II—DIFFERENTIAL DIAGNOSIS OF LIVER TUMORS

Means of manifestation	Benign	Primary malignant	Secondary malignant
Symptoms	Primary of pressure as vague local distress, indigestion or gastric or duodenal displacement	Definite pain with invasion. Systemic symptoms with anorexia, weakness, anorexia. Hemoptysis from esophageal varices or gastric invasion	Symptoms of tumor elsewhere that may be smaller than the liver metastasis. History of removal of possible primary
Signs	Palpable abdominal mass is firm, movable, solitary and rarely tender	Tumor mass is fixed, hard, multiple and often tender	Discovery of tumors elsewhere often with little symptoms
Laboratory	Jaundice, obstructive, if bile duct occluded. Acolic stools. No urobilinogen. Van den Bergh immediate direct. Otherwise physiology undisturbed	Jaundice if hepatic failure with invasion. Stools \pm acholic. Strong urobilinogen. Van den Bergh is indirect. Anemia. Hypoproteinemia	Tests for significant disturbances. If tumor elsewhere as in urinary, gastrointestinal tract, bone marrow etc. Anemia. Hypoproteinemia
X ray	Localized mass in liver displacing other organs as stomach or duodenum	Invasion fixed mass in liver. Duaphragm elevated and often fixed	Search for tumor elsewhere as gastrointestinal tract, etc.
Biopsy	Visualization to show accessibility for resection	Visualization of invasion, multiplicity. Rarely resectable	First of all possible sources including suspicious ovary. Later of liver mass to discover its source

diagnosis carried out therapeutic measures which leaves one to assume a correct preoperative diagnosis was made. Hence the results can be stated thus: Preoperative diagnosis was correct or not stated in 73.2 per cent. preoperative diagnosis was wrong in 26.8 per cent.

At the Cincinnati General Hospital 47 cases of clinically manifest adenomas and carcinomas of liver cells have been studied microscopically. Of these 33, or 70 per cent. had a correct clinical diagnosis before operation or autopsy.

Differential diagnosis is admittedly difficult but often possible when all factors are considered together and for that reason the following diagnostic table is included.

TREATMENT

Adequate noninjurious hemostasis has been the major problem in surgical treatment and the subject of experimental work. That success experimentally is no guarantee against failure when applied clinically was shown as early as 18,9 when Tillman controlled bleeding with ease by simple pressure after ligation of major cut vessels in resected livers of animals. Attempt by Escher to apply this clinically resulted in fatal hemorrhage. The human liver with a pathologic lesion differs by being abnormally friable and highly vascular. Tamponade in various forms, application of hemostatic substances, and reduction of blood supply by tourniquets or clamping about the liver or hepatoduodenal ligament are not entirely successful. Cautery hemostasis proved useful only when it was controllable as by electrocoagulative methods. Hemostatic sutures proved most effective experimentally as well as clinically. Substances used to prevent sutures from cutting into liver tissue have not proved practical. The introduction of blunt needles that push aside blood vessels

rather than penetrate them with consequent bleeding was a real contribution by Kousnetzoff and Pensky.

Indications for surgical removal of primary tumors of the liver depend upon their size, their location with relation to major bile ducts and blood vessels at the hilum of the liver and upon the general condition of the patient including the condition of the rest of the liver. The majority of authors (Scheleff, Tinker, Gray, Cullen, Tuffier, McArthur, Fevre and Dassios) believe resection is indicated in adenomas, cystadenomas, localized solitary carcinomas, and hemangiomas but with the following restrictions: no lymph node metastasis should be demonstrable as in the regional nodes along the vessels at the liver hilum; the tumor should not involve the major blood vessels nor bile ducts at the hilum (Ward) and there should be no marked reduction of hepatic function indicative of extensive involvement of the liver parenchyma (Walton, Nadler and Wolfer). In addition in cases of cystadenomas one must decide whether to marsupialize or resect completely and also one must rule out generalized cystic disease that involves other organs as well. There are surgeons with two extremes of opinions: those who believe surgical intervention is very rarely feasible (Crile, Cole, Alessandri) and those who optimistically resect extensive primary carcinomas with involvement of adjacent organs or even known secondary carcinomas (McArthur, Cattel, Cullen). At the Cincinnati General Hospital an exploratory laparotomy is done when symptoms, signs, x ray and laboratory findings are those of a freely movable tumor of the liver without evidence of metastasis, without marked hepatic insufficiency and without a grave operative risk. Actual resectability can best be determined during the exploratory laparotomy.

mission to the hospital, when she noted a dull pain in the right upper abdomen that extended posteriorly to the inferior angle of the scapula where it was most marked. At the same time she noted a mass in the right upper abdomen that remained unchanged. She felt distended after meals with occasional nausea. There had been no vomiting, jaundice, nor loss of weight. Examination was negative except for the 8 centimeter mass attached to the liver assumed to be of gall-bladder origin.

Operation—performed on November 28, 1934, by Dr. Mount R. Reid. Ether-oxygen anesthesia was used. Through a right rectus incision an 8 centimeter mass was revealed, covered by adherent omentum and attached to the right lobe of the liver by a 5 centimeter base near the fundus of the gall bladder. The cystic duct was divided and the gall bladder freed to point near the tumor. Two rubber-shod clamps were placed across the liver radiating from the hilum proximal to the tumor and (64) interrupted mattress sutures of chromic catgut were placed for hemostasis longitudinally proximal to the clamps. The tumor was then excised with electrocautery and the clamps removed. The cut edges were sutured together with No. chromic catgut suture supported by the longitudinal hemostatic sutures. A cigarette drain was placed down to the stump of the cystic duct and the incision closed.

Postoperatively there was considerable abdominal distention for 3 days, relieved by enemas and pituitrin. The drain was removed on the 4th postoperative day and she was discharged from the hospital on the 10th day in very good condition. She has been seen repeatedly at frequent intervals and has remained in good health over 8½ years, with no signs and symptoms.

Microscopically the tumor was typical adenoma of liver cells completely encapsulated.

CASE 3. C. G. H., No. 6538, A. D. this patient, 38 year old negro, began to have pain in the middle of the back July, 1929, 7 months before admission to this hospital. In October, 1929, he noted a golf ball sized, slightly tender epigastric mass that moved with change of position of the body. He went to several physicians and was given medication without improvement. He was worried and lost 20 pounds in 6 months. An exploratory laparotomy and biopsy of the mass was done March, 1934 at another hospital. He was told that he had an inoperable carcinoma of the liver. He continued to lose weight while seeking treatment elsewhere and entered this hospital November 1934. Our review of the microscopic slide of the biopsy led to diagnosis of an adenoma of liver cells.

Operation was performed November 5, 1934, by Dr. B. N. Carter. It was done through a transverse incision that crossed the right rectus scar of the previous operation and a T-extension was made along the old scar for better exposure. Adhesions had formed between the old scar and tumor to the anterior abdominal wall and the transverse colon and omentum. The structures were freed and the liver tissue compressed by the fingers of the assistant while the tumor was progressively resected with Bowle unit and suture across the line of incision with No. chromic catgut as carried out as the resection progressed. Six cigarette drains were placed down to the charred edge of the liver and the closure of the abdominal wall was re-enforced with silver wire stay sutures. Postoperatively he developed bronchopneumonia, which responded well to sulfathiazole therapy. The thick discharge from the eschar obstructed the drains so that on the 7th day his temperature again rose to 106 degrees. Round rubber drains replaced the cigarette drains and proved to be adequate but he continued to have persistent discharge from the wound for over weeks until the sinus finally closed. Since that time he regained his weight and has been in good health without signs

of recurrence now for over 29 months since the resection of his tumor.

The tumor measured 13 by 9 centimeters and was completely encapsulated. Microscopically it was a typical adenoma of liver cells (Fig. 6).

A review of all reported resections of liver tumors totals 223 cases with complete description of operations as well as microscopic confirmation of diagnoses. Notable reviews of the past include those of Keen, 1892, 1897 and 1899; Anshutz, 1903; Cullen, 1905; Schroeder 1906; Garre, 1907; McDill, 1912; Thole, 1913; Yoernan 1915; Timber, 1935 and Charache, 1939. Since the number of resections performed by any one surgeon are very few, a review of all reported cases offers the only way of adequate comparison of the various methods of resection.

There remain 347 resected cases that could not be included in tabulating and evaluating treatment because the referring authors did not give the source of the report mentioned, became some references were incorrect, some were in unobtainable journals, and a large number did not give adequate information about the case or the diagnosis was questionable. These include 173 resected cases of primary carcinoma of liver cells, 34 resected cases of primary sarcoma of the liver, 26 resected cases of solid adenomas of the liver, 8 resected cases of gall-bladder carcinoma involving the liver, and 6 or more resected cases of cystadenomas of intrahepatic bile duct origin. If all these cases could be accepted, there would be a total of 570 resected cases of liver tumors.

There are 6 common postoperative complications for which the surgeon must be on the alert. (1) Blood loss is no longer as much a danger as it was, for in Keen's review (1899) of 74 cases there were 11 deaths, of which 8 or 73 per cent were due to hemorrhage. Since the beginning of this century in 149 cases resected there were possible manifestations of bleeding with fatality in only 3 cases (Mantle, 1903; Parin 1913; Ramsey 1929) and of these only 1 a hemangioma, had gross hemorrhage. (2) Infected wounds, peritonitis and septicemia are also much less important than in the past. (3) Prevention and chemotherapy have minimized the importance of respiratory complications such as pneumonia and atelectasis. (4) Three forms of metabolic disturbances giving rise to postoperative difficulties are (a) liver shock (Ravdin) or liver deaths (Sutton) which occur earliest, (b) hepatorenal syndrome and (c) general malnutrition largely as hepatic hypoglycemia which occurs late. (5) Postoperative ileus and at times hematemesis follow clamping of hepato-duodenal vessels with engorgement of portal cir-

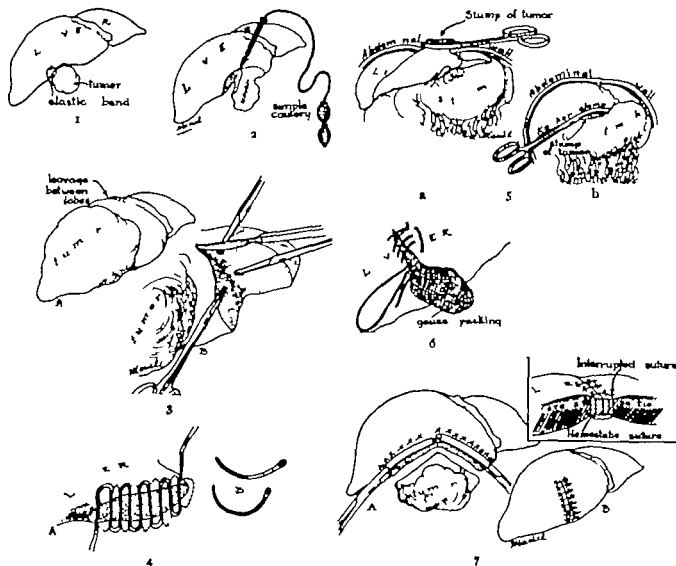


Fig. 2. Major methods of resection. (1) Elastic ligature and extraperitonealization of the stump (Cousins, 1874). (2) Simple cautery (Parquellin) removal (Echer 1886). (3) Lobectomy with reported less bleeding for physiologic line of cleavage used (Langenbuch, 1888). (4) Hemostatic suture with blunt needle and closure of liver surfaces after resection (Kousnetoff and Penaky). (5) Clamps left on for hemostasis and, a, completely exteriorized (Lapoint, 1897) or b, only the handles exteriorized for removal through a stab wound (Kocher 1903). (6) Excision with tamponade (Anschütz, 1903). (7) Hemostatic sutures placed proximal to clamps and electrocautery excision of tumor distal to clamps. Raw surface closed by interrupted sutures going around the longitudinal hemostatic sutures preventing cutting of sutures through liver tissue. This method was used in Case 2.

culation (6) Persistent sinuses occur with discharge of bile after marsupialization of cystadenomas, with discharge of necrotic slough from an excessively thick eschar of cautery or with discharge of pus from tracts left by drains.

SUMMARY AND CONCLUSIONS

A practical classification of primary tumors of the liver is presented with definition of terms. Emphasis is placed on the pathologic differentiation of true adenomas that are resectable with a good prognosis.

Clinical diagnostic features stress the local manifestations of benign tumors in contrast to the

systemic disturbances of malignant tumors particularly those that are inoperable. Bile duct carcinoma tends to be more rapidly fatal and anaplastic than those of liver cell origin.

Diagnostic error clinically was less than 30 per cent. A table of differential diagnosis between benign tumors, primary carcinoma, and secondary malignant tumors is given.

Treatment of liver tumors must be entirely surgical to be successful. X-ray therapy is not only ineffective but detrimental. Surgical resection should be attempted in all localized liver tumors without evidence of involvement of adjacent organs or too much of the liver itself and should

be deferred until the patient is in best possible condition. After proper preparation the best method of resection appears to be a combination of hemostatic sutures and electrocautery.

Review of literature indicates that 223 resected cases have been fully reported but the probable total number of cases is about 570 when those of limited description are included. It is apparent that the operative mortality is not high but most failures are due to inadequate removal with recurrence.

Postoperative complications are largely those of metabolic disturbances such as early "liver deaths," late "hepatorenal syndrome," or finally malnutrition with loss of resistance to infection. These are preventable.

In conclusion an attitude of futility should not be entertained toward all patients with primary liver tumors.

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EDITORIALS

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JUNE, 1945

THE CLINICAL USE OF BORIC ACID

OUR medical journals and daily newspapers announce with grim regularity the tragedy of death from boric acid poisoning in hospitals and clinics all over the country. And it is obvious that the reported cases though seemingly numerous do not constitute the aggregate of victims suffering this tragedy. Evidence that the problem has exceeded the academic stage of discussion is indicated by the fact that the toxicity of this compound was brought up for discussion at the recent National Chemical Exposition and one state legislature already has up for consideration a statute to outlaw its unprescribed use.

The poisonous nature of boric acid was recognized as early as 1883 when Brose reported a death following its use as a dusting powder on a chronic leg ulcer. Subsequent reports have demonstrated its toxicity when absorbed from the gastrointestinal tract or when administered parenterally and poison-

ing has been described in infants who have suckled from nipples cleansed with saturated boric acid solution. There have been reported numerous deaths due to the absorption of the drug from cavities such as the pleura, that have been irrigated with solutions of boric acid in the treatment of infections. Recent investigations by the Naval Medical Research Institute have demonstrated that boric acid whether applied in the form of a saturated solution or as an ointment is absorbed from extensive wounds or burns and is a cumulative poison.

Investigation into the mode of administration in fatal cases discloses that in some instances poisoning occurs when the physician who prescribes it does not know of the harmful nature of the drug while in other instances the toxic substance is unintentionally substituted for an innocuous solution. Typical accidents that have occurred repeatedly are the intravenous administration of boric acid solution in the place of glucose or saline solution which had been prescribed and the preparation of infant feeding formulae with boric solution instead of sterile water. The frequency of such unwitting and accidental poisoning suggests that the universal employment of boric acid today constitutes one of those habits acquired by inheritance—and never critically evaluated.

The medical profession has used boric acid since Joseph Lister in 1875 in his communication entitled *On Recent Improvements in the Details of Antiseptic Surgery* first described its use in clinical medicine. Lord Lister had employed it himself first in the treatment of an onychia on his little finger. He observed that a dressing saturated with

boric acid was more soothing to his finger than one with carbolic solution and that the infection subsided promptly after its application. He concluded: Here then I had at once sufficient evidence that the new antiseptic, when employed in the form of a watery solution, was both highly efficient and much less irritating than carbolic acid. The general acceptance of this innocuous odorless and practically tasteless substance was no doubt enhanced when its mildness was compared to the robust character of the antiseptics that were the order of the day. Boric acid was soon

widely used for the dressing of wounds and for the irrigation of inflamed cavities.

The widespread use of boric acid solution today probably derives chiefly from the inertia of established custom and its clinical survival no doubt results more from its property of blandness than from any of its other attributes, for it is not a satisfactory antiseptic. On the basis of our present knowledge of its toxic properties boric acid should be regarded by the medical profession as a poison and should be handled as such.

REED M. NISBET

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE third edition of *Interns Handbook*¹ is a small volume planned to fit the coat pocket of its owner yet supposed to contain a complete summary of medical and surgical therapeutics. Its opening pages deal briefly with instructions for the interne concerning his duties and responsibilities in hospital life. This is followed by a section on medical laboratory techniques. The third and fourth parts are given over to medical and surgical procedures, while the last section concerns itself with a description of numerous drugs and biologicals.

In general the aim at completeness in scope has resulted in an unbalanced spread of details. An attempt has been made to cover all disease entities with no heightened emphasis upon situations which commonly arise. The chief example of its sparseness of detail is the section on surgery where only general outlines are given, while the rarest of medical situations appear to be very well anticipated. While brevity is the byword throughout, the sections on laboratory techniques and pharmacology have used space which otherwise could have been devoted to clinical procedures whose details often are hidden in the literature yet are well known to more experienced practicing physicians. There is no doubt but that the text has merit because it is such a compilation but one feels that it will be more satisfactory to a senior medical student just starting his hospital experience than to an interne who is about to accept a greater degree of responsibility.

This text cannot supplant the average hospital procedure book, but in the absence of the latter it will be an aid to the unguided interne who feels the need of readily available pocket information.

WALTER W. CARROLL.

IN the fourth edition of the former *Manipulative Surgery*² many additions and alterations have been made and some sections have been largely rewritten. A number of new illustrations of manipulative technique have been added.

Misapprehension frequently exists among the profession as to what manipulative treatment means and what it can achieve. There is also a tendency to emphasize unduly the dangers of manipulation. This book shows exactly what treatment by manipulation means and that intelligent discrimination is as necessary in this as in any other branch of surgery.

INTERNS HANDBOOK. By members of the Faculty of the College of Medicine, Syracuse University. Under the direction of M. D. Dealey, A.B. M.D. and Maynard E. Holmes, M.D. F.A.C.P. 3d ed. Philadelphia, London, and Montreal: J. P. Lippincott Co. 944.

TREATMENT BY MANIPULATION IN ORTHEDIC AND CONJUNCTIVE PRACTICE. By A. G. Tibbitts Fisher, M.C., M.B. Ch.B. F.R.C.S. (Eng.). New York: Paul B. Hoeber Inc. 944.

This subject is not sufficiently emphasized in the curricula of our medical schools. Cures by manipulation are so many and so well authenticated that the subject demands the fullest investigation. The subject should be taught by lectures upon the underlying pathology and by actual practical demonstration in our medical schools and hospitals. Interest and enthusiasms must be aroused. Research must be conducted into underlying physiological and pathological principles. Careful records must be kept. These procedures should be easy for every out-patient department contains cases which urgently need manipulation.

This book points the way to accomplish good results by manipulation. Surgeons should read this book to see what the author, an orthopedic surgeon, believes treatment by manipulation will accomplish.

JOHN S. COULTER.

SOME investigators have recognized a relationship between immunochemistry and enzyme chemistry yet physiological chemists in general have paid little attention to immunity and conversely immunologists have had small interest in the chemistry of enzyme action. *Immuno-Catalysis*³ by M. G. Sevag is an able elucidation of the author's theory of immunocatalysis. He demonstrates by an extensive and wise use of the literature the many parallelisms between protein antigen and enzymes and between antibodies and antisymes and by integration that antigens show properties which satisfy the well known criteria of catalytic agents and that specific antibodies formed as final reaction products in response to antigenic stimuli fulfill the function of specific inhibitors of enzymes. The book will especially interest immunologists and biochemists and act as a challenging incentive to further research. It is an excellent review of the literature with an exceptional bibliography.

A. A. DAY

BECAUSE of the outstanding qualities of the authors and widespread acceptance of their leadership in this field, it may seem unnecessary to review the book *Essentials of Oral Surgery* by Blair Ivy and Brown⁴ who, in long association, have been authoritative teachers of surgery and diseases of the oral cavity.

The arrangement of the material in the book conforms to that of Blair's original text *Surgery and*

¹INTERNS-CA ALBERT. By M. G. Sevag, Ph.D. Springfield, Illinois, and Baltimore: Maryland: Charles C. Thomas. 945.

²ESSENTIALS OF ORAL SURGERY. By Wilbur Fyfe Blair, A.M. M.D. F.A.C.S. and Robert Henry Ivy, M.D. D.D.S. F.A.C.S. with the collaboration of James Barrett Brown, M.D. F.A.C.S. 3d ed. St. Louis: The C. V. Mosby Co. 944.

Diseases of the Mouth and Jaw published in 1912 and much of this material has been retained. The new book, with the collaboration of the present authors, has been brought progressively up to date to the present third edition.

Primarily intended as a text and guide in surgery for dental students the book maintains that objective and further provides a valuable source of information for medical students and practitioners on a subject rather neglected in medical education. The scope of the book is tremendous and most revealing to one not particularly familiar with the diseases and affections to be found in the oral cavity.

Particular importance is attached to the need for recognition of surgical conditions and, while the opening chapter deals exclusively with examination, anatomical considerations, and study leading to diagnosis, this emphasis is stressed throughout the book. This sound approach to the subject is founded on the unusual combination of abilities of these individual authors as teachers, clinicians, and resourceful surgeons. In this book the dentist will find the solution to his most disturbing problems—those concerned with acute and chronic infections and inflammatory conditions arising about the teeth,

fractures of the jaws, dislocation of the jaw and the loss of teeth or roots in the antrum.

The chapter written by Dr. Kazanlian on the surgical preparation of the mouth for artificial dentures will be particularly appreciated by the dentist who is anxious to improve the efficiency of his prosthetic efforts.

With the exception of the chapter on fractures of the jaws, that dealing with tumors is given most space (68 pages). This is one of the most important chapters in the book and the emphasis laid on pre-cancerous lesions and cancer of the mouth and jaw bones is desirable and commendable.

The rôle of the dentist in the control of cancer is definite, and the plea is made for fundamental knowledge of oral pathology and a routine and complete survey of the whole mouth.

New material has been included to bring the sections on shock, hemorrhage, burns and wounds up-to-date. Developments in the treatment of fractures are described and illustrated.

This book of 624 pages, with 467 uniformly good illustrations, is a desirable textbook for dental students and medical students, and deserves a place in the library of every surgeon and dentist.

FREDERICK W. MERRITT.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

FIETOLOGIA ENDOCRINA. By Amado Ruiz Sánchez. Vol. 2. Guadalajara, México: Universidad de Guadalajara, 1944.

CLINICAL ROENTGENOLOGY OF THE DIGESTIVE TRACT. By Maurice Feldman, M.D., 2d ed. Baltimore: The Williams & Wilkins Co., 1943.

PENICILLIN THERAPY INCLUDING TYROTHRICIN AND OTHER ANTIBIOTIC THERAPY. By John A. Klumet, M.S., M.D., Dr. P.H., Sc.D., LL.D., LL.D. F.A.C.P. New York and London: D. Appleton-Century Co. Inc., 1943.

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THE FUNDAMENTALS OF ELECTROCARDIOGRAPHIC INTERPRETATION. By J. Bailey Carter, M.D. F.A.C.P. With a Foreword by Horatio Burt Williams, 2d ed. Springfield, Ill., Baltimore, Md.: Charles C. Thomas, 1943.

THE NEW BORN INFANT; A MANUAL OF OBSTETRICAL PEDIATRICS. By Emerson L. Stone, M.D. 2d ed. Philadelphia, Lea & Febiger, 1943.

CLINICAL CYSTOSCOPY: A TREATISE ON CYSTOSCOPIC TECHNIQUE, DIAGNOSIS, PROCEDURES, AND TREATMENT. By Lowrnan E. McCrea, M.D. F.A.C.S. Philadelphia: F. A. Davis Co., 1943.

DISEASES OF THE NERVOUS SYSTEM IN INFANCY, CHILDHOOD AND ADOLESCENCE. By Frank R. Ford, M.D. 2d ed. Springfield, Ill.: Charles C. Thomas, 1944.

AMERICAN COLLEGE OF SURGEONS

GRADUATE TRAINING IN SURGERY AND THE SURGICAL SPECIALTIES

CHARLES R. REYNOLDS M.D. Major General U.S. Army (Retired) Chicago Illinois

THE Surgeon General of the United States Army has announced that of the wounded who live to reach Army hospitals, more than 90 per cent are being saved. This is not entirely due to chemotherapy and the use of penicillin and blood and blood substitutes but to a large extent is the result of sound surgical principles applied to trauma. The surgical profession may well be proud of that accomplishment. Looking back over the road it has come, the profession knows that the surgical proficiency of today is the fruit of the decisive planning of yesterday through which the more or less haphazard apprenticeship system of training has been rapidly supplanted by scientifically set up well rounded programs of graduate training in surgery.

Right now when scientific surgery is being put to its supreme test is the time for surgeons to resolve that the unavoidable disruption of surgical education by the war must be compensated for at the earliest possible moment. The temporary setback must be repaired by postwar plans so complete and progressive that they will take up the wartime lag and reinstate surgery on its former march.

Dr Dallas B. Phemister chairman of the Committee on Graduate Training in Surgery of the American College of Surgeons said in an article in the February 15, 1942 issue of SURGERY GYNECOLOGY AND OBSTETRICS: "The needs of our military forces must be met and under the present world conditions some of our most desirable and ambitious plans may have to be changed. The prediction has come true. We have had to curtail training in surgery at a time when we urgently need more and better trained surgeons. A decreasing number of trainees have been permitted to carry their educational programs through to completion. As the months pass and the war lengthens the situation becomes increasingly grave."

Consultant in Graduate Training in Surgery American College of Surgeons.

EFFECTS OF PRESENT WAR ON MEDICAL EDUCATION

Under the Army specialized training program and the Navy V-12 program medical education on the undergraduate level has up to the present time been maintained on a reasonably normal basis considering the disruption of facilities and hospital staffs. The accelerated program has made possible the graduation of 5,500 doctors every 9 months or at the rate of 7,000 every 12 months. Of course, the majority of the war time graduates enter military service after a 9 months' internship. The induction of premedical students will result in a decrease in graduates, and by 1948 and 1949 in shortage of physicians, calculated on a prewar basis.

Under the 9-9-9 plan hospitals may retain for a 9 months assistant residency one-third of the men who complete the 9 months general internship and may keep for a further 9 month period one-half of those who complete an assistant residency. As Dr Frank Lahey chairman of the Directing Board of the Procurement and Assignment Service has said, "The 9-9-9 program is working fine but no one likes it. Inadequate training is given the young men and they are not qualified under it to go out and practice medicine of a standard that the medical profession has set. It is a makeshift and compromise system which is one of the sacrifices that it has been necessary to make to win the war. Its faults make it the more urgent that plans be set up for further training of these men when the war is over. The abbreviated or hurried curricula in medical schools, the depletion of school facilities and hospital staffs, and the abbreviated internships and curtailment of training at the residency level all conspire to set back medical education in this country not only during the war but for several years afterward."

Great credit should be given to medical schools and teaching hospitals which have carried a heavy load of undergraduate and graduate education with depleted staffs.

PROFESSIONAL EXPERIENCE WHILE IN MILITARY SERVICE

As in all recent wars great advances in medical science are being made in this one. These have become evident in preventive medicine, treatment of tropical diseases, in chemotherapy and the use of penicillin in medical and surgical conditions, the use of blood and blood substitutes, in traumatic surgery and the control of wound infections and the treatment of burns and in the broad field let us call it reconstruction surgery wherein are to be included orthopedic, vascular, neurological, and plastic surgery and physical medicine.

By reason of concentration in large hospitals the casualties of war are conveniently arranged for medical and surgical practice and research on a very broad scale. Where in peacetime are to be found hospitals of 5,000 to 10,000 beds set aside for the care of special diseases and injuries? It is safe to say that there are several Army hospitals which are now caring for more neurosurgical cases than all the civilian hospitals in the country combined. The same may be true, to a less extent, as to amputation, fracture, vascular orthopedic, and other cases for physical rehabilitation.

Unfortunately the great or overall advantages accruing to medicine as a result of this war are not participated in by a large proportion of the younger medical officers. When many of these men balance experience gained in the war against the loss of several years of training and practice, particularly if their specialty is surgery they will find themselves several years behind their programs of graduate training.

Senior medical officers naturally occupy the higher professional positions where they are privileged to preserve or advance their professional status. The junior officers, with exceptions, are assigned to troop duty or small medical units. This being the toughest war in history, the demand for the young and vigorous and the tables of organization which determine assignments naturally place a preponderance of young medical men with the combat forces. The recent medical graduates fall into this group. Those who planned or started a surgical career have certainly had their graduate training "impeded, delayed, interrupted or interfered with," as expressed in the subsection on education of the "G. I. Bill."

The scope of wartime medical and surgical practice in the Army except in some of the general and large area hospitals, is lacking in several important features which are necessary in a well rounded program of graduate training in surgery and the surgical specialties.

This is not to imply that all young medical graduates who enter the Army and Navy say goodbye to their graduate training plans for the duration. Those who are fortunate enough to serve in general or large area hospitals find themselves associated with specialists of the highest caliber drawn from medical schools, teaching hospitals and clinics. Clinical material, though not diversified to cover the entire field of surgical training is available. It is known that most of these hospitals are making a point to carry on comprehensive training programs for younger medical officers and otherwise to meet the "essentials" as laid down by the American Medical Association and the "standards" of the American College of Surgeons.

However surgery at the front is limited quite largely to emergency surgery in which many junior officers see only the early treatment and, except when serving with auxiliary surgical operating units, do not take part in the definitive operative procedures and the postoperative care and rehabilitation of war casualties.

The age of the patients is young, mostly males from 18 to 38, with the exception of officers. Consequently the medical officer gains relatively little experience with the conditions prevalent in middle and old age groups, such as the degenerative or chronic diseases—conditions becoming year by year more prevalent and of increasing importance to surgeons. There is also scarcity of experience in care of women and children, many getting no experience in obstetrics, gynecology and surgical conditions of children and adolescents. Their experience is extremely limited too regarding the chief causes of death—heart disease, cancer and apoplexy.

Another factor detracting from the educational value of medical experience in this war is the likelihood of prolonged absence from laboratory and research projects and from experience with the newer medical and surgical procedures in hospital practice.

It will be from this group of 18,000 or more younger medical officers, that requests for graduate training in surgery of a comprehensive type will come. Among its other objectives, the American College of Surgeons recognizes an obligation to develop programs and facilities that will make it possible for future Fellows to meet the requirements for fellowship especially in relation to graduate training in general surgery and the surgical specialties. Professional experience gained in military service will be evaluated and credit given by the College and the boards of medical specialties.

PROGRESS OF GRADUATE TRAINING IN SURGERY

At this point it might be well to trace the origin and development of the system of graduate training that is recognized today to constitute adequate preparation for surgery. Nearly 30 years ago at a meeting of the Southern Surgical Association, Dr Thomas S Cullen of Baltimore credited the American College of Surgeons with beginning remedial measures to control unwarranted operating by inexperienced men. That the most progressive minds in the profession were already thinking in terms of the extended training which all of us consider essential now is shown by the further remarks of Dr Cullen as follows:

"The medical student who after graduation decides to make surgery his life work should not take up his chosen specialty at once but should spend at least one year in a strictly medical service. A broad foundation in general medicine is absolutely essential. The following year can be most profitably spent in the pathological laboratory in making and cultivating the bacterial flora associated with them. After this he should become a surgical interne under a competent surgeon. His time will now be occupied in taking histories, assisting at operations, and in the after care of patients. He will also have ample opportunity for studying all tissues coming from the operating room. He thus has a complete picture of the patient's condition from the time of admission until his discharge, and from the laboratory findings has a clear idea as to the ultimate prognosis of the case. After he has assisted from one to two years, he is allowed to perform the simpler operations, and by the end of the second or third year he is competent to handle the more difficult cases. After a year or two as resident surgeon he is amply fitted to start out as a full fledged surgeon, with the definite knowledge on the part of the hospital that he will be a credit to the school and to the institution from which he has come."

Dr Cullen went on to say that a lack of knowledge of pathology "is the weakest point in American surgery today" and we agree with his conviction that to practice surgery without an adequate knowledge of surgical pathology is like building upon the sand.

Again and again through the years we find individual surgeons voicing the hope that the training of surgeons be placed on a scientific plane. The American College of Surgeons began to give the subject continuous consideration from 1930 on. In 1933 Dr William D Haggard told members of a Hospital Standardization Conference sponsored by the College that the most satisfactory preparation for a surgical career was a residency in surgery after a general hospital service in a university or other hospital for 2 to 5 years, combined with some teaching. In 1935, Dr Edward W Archibald in his presidential address to the American Surgical Association said in part:

"There has arisen in considerable numbers a certain type of surgeon which we all recognize and deplore. He is the natural product of those discoveries and inventions—an

esthesia, asepsis, fine tools, and well equipped small hospitals—which have rendered the practice of surgery in its purely mechanical aspects, relatively safe. He is progressive, venturesome, and self-confident, and such qualities are perhaps those which have placed the best of American surgery in its present proud position. But in the particular type to which I refer, venturesomeness becomes foolhardiness, and self-confidence is uncontrolled by knowledge. To such a man the sum of acquired knowledge is comprised in the popular theories of the year just past. Theory is counted as fact, the hypothesis as a thing proved. A decision to operate is based upon a medical catchword or a rule of thumb. Fingers replace brains, and handicraft outruns science. The result is that such a surgeon is apt to undertake operations which may be technically possible but which are scientifically unjustified."

Important developments with respect to stimulation of interest in proper training were organization of the American College of Surgeons in 1913 and formation of the specialty boards. The first specialty board the American Board of Ophthalmology was incorporated on May 3 1917 to examine candidates and to certify those who passed the examination. The American College of Surgeons provided office space and secretarial aid for the first two years of this Board's existence. Ophthalmology as a specialty in America began in 1855 when Elkanah Williams, of Cincinnati introduced the ophthalmoscope to this country and became the first American physician to limit his practice exclusively to ophthalmology and otology. Independent departments of ophthalmology and otology were established beginning with Cincinnati in 1860 Bellevue in 1868, Rush in 1869 Northwestern in 1870 Harvard in 1871 and Pennsylvania in 1872. Despite this academic recognition ophthalmology was treated like a step-child, S Weir Mitchell declaring in 1891 that he could remember the day in Philadelphia when older physicians refused to recognize socially a man who devoted himself to the eye alone.

In 1869 the Committee on Specialties of the American Medical Association resolved that this Association recognizes specialties as proper and legitimate fields of practice" but admitted that there were objections to specialties because they operate unfairly against the general practitioner in implying that he is incompetent to properly treat certain classes of diseases and narrowing his field of practice.

At any rate, specialization grew. In 1924 the board of otolaryngology was established in 1930 the board of obstetrics and gynecology in 1932 the board of dermatology and syphilology and in 1933 the board of pediatrics. Three boards were established in 1934 orthopedic surgery psychiatry and neurology and radiology. The board of urology was established in 1935 the boards of pathology and of internal medicine in

1936 the boards of surgery and of plastic surgery in 1937 the board of anesthesiology in 1938 and the board of neurological surgery in 1940

THE AMERICAN COLLEGE OF SURGEONS PROGRAM

The American College of Surgeons appointed a committee in 1928 to study what the requirements should be for training in surgery. They contributed a great many ideas. Finally in 1935 a committee under the chairmanship of Dr Samuel Harvey New Haven, professor of surgery Yale University Medical School, brought in a report supplemented by related reports by the associate directors of the College, Dr Bowman C. Crowell and Dr Malcolm T. MacEachern. Out of this study came the present plan for the promotion of training in surgery. This was followed by surveys in 1937 and 1938 for the establishment of a Minimum Standard, now used in the promotion of the work of graduate training in surgery and reproduced in this article.

A list of hospitals of the United States and Canada approved for graduate training in surgery was published first in January 1939. The "Approval Number" of the *Bulletin* of the College published in October 1940 contained a list of 300 hospitals which met the Minimum Standard for graduate training in surgery and also a directory of the approved plans including detailed descriptions of the provisions for basic science study, supervision and the gaining of practical experience. The directory was the first presentation of selected graduate training programs that had ever been made available to the graduate in medicine as a guide in his plans for qualifying himself to practice surgery. It makes possible careful selection of the institution which offers the program best suited to the individual's needs and offers ready opportunity for comparison of programs of different institutions. The new edition of the directory which will shortly be issued will bring the most up-to-date information regarding the approved programs to medical officers looking forward to demobilization and resumption of training. Other information of this nature will be imparted by the College upon inquiry received direct or through the information bureau of the American Medical Association.

One of the chief aims of the College in this program is to increase the opportunities for acceptable training in the moderately sized communities as well as the large medical centers, which will result in the distribution of surgical skill better suited to population requirements.

Preparation for the practice of surgery or a surgical specialty is so long and complicated a

process that careful planning is essential. It has been the experience of the American College of Surgeons in studying the qualifications of applicants for fellowship that a large proportion either fail to make suitable plans for training, or even from the course after they have embarked upon what would have been a suitable program. Advice is constantly being given concerning reconstruction of plans that have not provided the proper background. Considerable time must be spent with each individual advising and helping him with his problems, and the outlook is that the need for this service will be vastly increased when demobilization begins. The problems of evaluating experience while in military service will be added to those of appraising the training received prior to entering the service.

It is expected that physicians who will desire training in surgery after the war will be of 5 general types. These are listed as follows in the "War Issue" of the *Bulletin* of the American College of Surgeons, June 1944¹

1. Physicians who planned to specialize in surgery but who were commissioned immediately following their internships.
2. Physicians whose residencies in surgery were interrupted by military service.
3. Physicians who, under the g-o-g plan, were deferred, receiving one or two g-month periods of graduate training, and who will therefore require additional months of training to complete 3 full years following a 1 month's internship.
4. Physicians who in military service have received some training in surgery which, supplemented by further training, would be recognized as acceptable preparation for the practice of surgery.
5. Physicians with acceptable qualifications who had been in general practice prior to military service and who have gained a desire to specialize in surgery.

The American College of Surgeons, through its Department of Graduate Training in Surgery is pledged to give every possible assistance to the returning medical officer who desires to complete his training so that he may achieve his aim of meeting the criteria of fitness in the specialty of his choice.

Sixty thousand of the approximately 135,000 physicians engaged in active practice in the United States are serving with the armed forces. At present, some 18,000 of these are recent medical graduates whose training has been interrupted. An analysis of about 21,000 returns from the questionnaires sent to 60,000 medical officers by the American Medical Association indicates that four fifths want some kind of postwar training. Three-fifths indicate desire for long courses and one-fifth prefer short courses (less than 6

¹MacEachern, Malcolm T. Bull. Am. Coll. Surg. 1944, 49, 101.

MINIMUM STANDARD FOR GRADUATE TRAINING IN SURGERY

1 DURATION AND OBJECTIVE Graduate training in general surgery and the surgical specialties shall be of sufficient duration and educational content to enable the young surgeon upon completion of such training to begin the practice of surgery in a scientific manner. An acceptable program requires a minimum of two and preferably three or more years.¹

2 ORGANIZATION AND SUPERVISION (a) The medical staff shall be organized with heads of departments and a representative committee responsible for the organization of the graduate training program and for the personal supervision and direction of the work of the resident staff. (b) The hospital shall keep such records of the activities of the resident staff as may be necessary to assure an equitable distribution of work, and together with some form of examination provide a basis upon which the plan of graduate training may be evaluated.

3 BASIC MEDICAL SCIENCES (a) The hospital shall maintain a clinical laboratory an x ray department and other adjunct diagnostic and therapeutic facilities essential for diagnosis and treatment. Facilities for other basic science study, research and investigative work are desirable. (b) All services shall be under the continuous supervision of accredited heads of departments and have qualified technical assistants. (c) The resident staff shall be

required to observe and participate in autopsies to devote adequate time to the study of gross and microscopic pathology, to acquire a degree of practical knowledge of clinical roentgenology and radiology to pursue anatomical studies by dissections on the cadaver and animals to participate in clinical or experimental research or to devote definite time to other study of the basic medical sciences.

If not available within the hospital, provision for adequate collateral study of the basic medical sciences shall be provided through affiliation with another hospital or educational institution.

4 CLINICAL MATERIAL (a) The hospital shall have an active surgical service and an organized outpatient department with systematic follow-up clinics. (b) The number of patients shall be adequate to give the resident staff opportunity for training and experience in the diagnosis, treatment, and study of end results of a variety of surgical conditions. (c) Operative experience under supervision sufficient to obtain a degree of technical efficiency shall be provided for the resident staff.

5 ORGANIZED STUDY (a) The hospital shall provide a medical library containing a wide range of standard textbooks, current medical journals and periodicals with a librarian in charge. (b) A definite program of reading of scientific literature under guidance of the medical staff shall be required, and the resident staff shall take an active part in general staff conferences, departmental conferences, clinicopathological conferences and be responsible for some teaching activity.

¹Since the Minimum Standard was adopted, the Committee on Graduate Training in Surgery has agreed that the duration of an acceptable program should be three or more years following internship; this change in Clause I awaits the official consideration of the Board of Regents.

months) Applying these factors to the total of 60,000 it will appear that 48,000 medical officers now in service will look for postwar training.

The following are extracts from the report of the replies sent to medical officers in the armed services as compiled by Lieutenant Colonel Harold C. Lueth, M.C. Surgeon General's Office Liaison Officer American Medical Association.¹

"Requests for short courses included all specialties. The largest number of requests were for the following specialties in order of frequency: internal medicine, surgery, general review, obstetrics and gynecology, pediatrics, otolaryngology and ophthalmology.

The 10 most popular special fields of training by means of long courses, in order of frequency of request, were surgery, internal medicine, obstetrics and gynecology, general review, psychiatry and neurology, pediatrics, orthopedic surgery, ophthalmology, radiology and otolaryngology.

"Nearly two-thirds of the group, 73,333 or 63 per cent, expressed a desire to become certified specialists. There were 3,324 medical officers, nearly 16 per cent of the entire group, already certified by the American specialty boards. The remainder either did not care to be certified or did not mention their desires.

¹Am. M. Ass. 945, 7-63

"Nearly 40 per cent, 8,734 medical officers, came from private practice to the military services. Twenty-two per cent, 4,640, came directly from internships—nearly 10 per cent, 3,191 came directly from residencies, and the remainder came from various types of practice. About 15 per cent failed to answer the question concerning their previous type of medical practice.

"A comparison of the results of a pilot questionnaire and the present questionnaire was made. Long courses were requested by about one-fifth more in the final questionnaire than in the pilot questionnaire. Only two-thirds as many men requested short courses in the final questionnaire as in the pilot. The difference was attributed to a change of viewpoint of medical officers during the interval between the circulation of the questionnaires rather than to an error in sampling."

Very significant in this report is the number of medical officers who entered military service directly from internships—22 per cent—and 10 per cent additional directly from residencies.

The importance of training for demobilized physicians is well expressed in the interim report to the Senate Committee on Education and Labor from the Subcommittee on Wartime Health and Education dated January 2, 1945, quotation from which follows:

the accelerated undergraduate courses, and the shortened internships and residencies, will make it necessary to provide further supervised training for many recent graduates unless the future quality of medical and dental practice is to be jeopardized. Most of the young graduates are well aware of this. Neither the need nor the demand for postwar advanced medical training can be met with the graduate teaching facilities and staffs now available in medical schools. Expansion of such facilities through increased provision of teaching hospitals and medical centers, as part of the program hereinafter described and recommended, will therefore be required.

As new medical graduates go into service after the abbreviated 9 months internship and as current graduates, postwar, swell the numbers of those wanting and needing surgical training it becomes obvious that hospitals will be swamped with demands for training appointments when demobilization begins. It is fair to assume that at least 15,000 medical officers now in service will require some kind of surgical training at least 10,000 of whom will require extended training in surgery and the surgical specialties. There will be at least double the number of applicants for training than could be accommodated in the 235 hospitals which after survey and careful study of the findings have been approved by the American College of Surgeons for graduate training in surgery and the surgical specialties. Those hospitals are organized at present to train about 1,234 surgeons, with a possible expansion in the crisis to 1,900. Among these are the hospitals connected with medical schools which have been carrying the major load in graduate education and have been getting excellent results. They cannot accept much more responsibility. Their contribution must be supplemented by the educational efforts of non-university connected hospitals. Therefore about 250 additional hospitals must be assisted in creating a total of approximately 3,000 residencies in surgery to be ready to meet the expected requirements of those now with the armed forces. This places the problem squarely before us of surveying a total of at least 500 hospitals. The rate of release from military service, though not yet known is quite certain to result in a substantial demand soon after the cessation of hostilities in either major theater.

To further the program the Department of Graduate Training in Surgery has been expanded. On October 1, 1944, Dr. George H. Müller, formerly dean of medicine, American University of Beirut, Lebanon, Syria, joined the staff as director of educational activities. At the same time, the writer was appointed consultant in graduate training in surgery. Dr. Paul S. Ferguson who has been on the College staff for a number of years and has been in charge of surveys for gradu-

ate training in surgery was appointed director of surveys. The field staff for survey work will be enlarged to include at least 4 competent assistants. In addition the field men making the regular Hospital Standardization surveys under the direction of Dr. E. W. Williamson, assistant director of the College, assist with the work in graduate training in surgery. The associate directors, Dr. Malcolm T. MacEachern and Dr. Bowman C. Crowell, are very active in the work.

In undertaking this program the College has had rich experience over a period of 27 years in its Hospital Standardization program and has obtained valuable data upon which to base its program for graduate training in surgery. It has on file about 60,000 reports of hospital surveys.

Although general principles governing educational content of the training plans have been laid down in the Minimum Standard which accompanies this article, no set pattern can be developed because of the wide variations between the institutions which can furnish acceptable training. After certain fundamental requirements are met, there is room for considerable latitude in the details of operation. The essentials are concerned with duration, which must be not less than 3 years following internship, organization and supervision, which implies a well organized medical staff including exclusive specialists in their respective fields who possess teaching ability and who are given definite teaching responsibilities including supervisory duties and the selection and examination of graduate students, ample provision of facilities for and supervision of basic science study, an active surgical service, an organized outpatient department, and sufficient patients to provide ample clinical material and operative experience, under supervision, for the resident staff and provisions for organized study through a medical library and a definite program of reading and scientific reviews, in addition to participation in general staff, departmental and clinicopathological conferences, and opportunities for some teaching activity on the part of residents.

Within this framework there is room for individualization according to the type of institution, whether it be the large hospital directly connected with a medical school, the small hospital which arranges affiliations with other hospitals for broader clinical experience and with a medical school for basic science study, or the clinic which adds to its well set up apprenticeship type of training closely supervised by thoroughly qualified surgeons the benefit of facilities for study of the basic medical sciences and research.

The greatest obstacle to most hospitals in setting up graduate training in surgery programs is an arrangement for study of the basic medical sciences. It is difficult to lay down a definite program for graduate training in the basic sciences as there still exists a difference of opinion as to just what constitute the basic sciences in relation to surgical training or at least to what extent and when these should enter into the graduate program. Authorities, however seem to agree that they include anatomy physiology biochemistry pathology, bacteriology and roentgenology and that at the graduate level they should be taught by the applicatory system so far as possible. Some believe that they should be taught over a period up to 12 months at the beginning of the training program or in a subsequent year whereas others believe this training can be obtained throughout the several years of residency in hospitals well organized for educational purposes. The latter lean especially to the idea of the resident obtaining this training through special research projects so far as practicable. Perhaps the consensus is that so far as pathology and roentgenology are concerned, hospitals which have competent pathologists and radiologists on their staffs may be able to arrange teaching programs right in the hospital throughout the residency. The same is true of biochemistry and bacteriology which can usually be taught by practical experience in the laboratories. For the teaching of anatomy and physiology on the other hand, definite medical school affiliations are most desirable although there will be cases of hospitals which can furnish excellent resources for study even in these subjects. In general, however hospitals cannot provide opportunities for cadaver dissection due either to lack of facilities or to legal restrictions.

In approving hospitals for graduate training full consideration is given to all of the factors involved in a given situation with proper credit for resourcefulness in devising ways of giving the students adequate training—there is no set pattern that will govern all cases, and no intention to handicap certain hospitals by adhering to a rigid, specific plan that they cannot possibly meet.

Studies now being made by Dr. George H. Miller of the College staff by personal visits to selected medical centers in the United States and Canada to study existing plans and further possibilities for co-ordination of graduate training between hospitals and medical schools will throw much light on the means of solving the problem of the basic medical sciences an up-to-date knowledge of which will be especially valuable to those returning from military service. Under all

circumstances it is essential for a man preparing to become a competent surgeon to know the fundamental sciences. To ignore the applied sciences in the scheme of training would lower the standards of surgical practice.

The picture before us is the medical veteran returning home after making a substantial and costly contribution to his country's security. He is asking and will expect, to re-establish himself in the study or practice of surgery in the most approved scientific way. From the standpoint of patriotism alone that obligation on our part is a compelling one. If this situation is not met substantially as the College proposes to meet it, the result will be distressing disillusionment, occasioned by many young medical men having to go into practice without completing their plans for special training and a serious setback to the standards of surgical practice so substantially advanced in this hemisphere in recent years.

Another consideration is that medical education has been practically suspended in many of the countries of Europe and Asia. For years to come the United States and Canada will be looked upon as centers for postgraduate medical education to meet the requirements of students in war torn countries as well as those from South and Central America who even before the war had begun to seek training opportunities in North America.

THE G. I. BILL

The financial problems of the demobilized physician who wishes to resume his training will be somewhat simplified by the Service Men's Readjustment Act, popularly known as the G. I. Bill which was approved on June 22, 1944. Under this Act a veteran while enrolled in and pursuing a course of education or training in an educational institution which term includes teaching hospitals may be paid a maintenance allowance of \$50 per month if without a dependent, or \$75 per month if he have a dependent or dependents. Medical schools and hospitals may also receive up to \$500 a year to cover cost of tuition laboratory fees books supplies and equipment exclusive of any charge for maintenance for each student who is accepted for training under the G. I. Bill. To be eligible for educational benefits the discharged veteran must have been in active service not less than 6 months, or shall have been discharged or released from active service by reason of an actual service incurred injury or disability.

GRADUATE TRAINING IN GOVERNMENT HOSPITALS

The College has surveyed 31 United States Naval Hospitals 9 United States Public Health

Service hospitals, and 20 Veterans Administration hospitals, to determine their qualifications for graduate training in surgery. It seems impracticable to establish comprehensive programs of training in Army hospitals under existing military conditions, but such training may be considered as a postwar program. However short courses of training "on the job" for volunteers are now being carried on in selected hospitals, chiefly for the benefit of medical officers who have been on administrative duty or in combat areas where opportunity for professional service has been lacking. Plans are now under way to establish graduate training programs substantially as formulated by the American College of Surgeons extending over a period of 4 years, less credit for worthwhile experience, in a number of hospitals of the Navy, the United States Public Health Service and the Veterans Administration. What has been said before regarding the clinical material in service hospitals available for surgical training should be borne in mind in estimating this feature of the program of the College.

It is likely that long or comprehensive programs of training will be established when the military situation clears. Such programs will be an inspiration to officers to carry out their purpose to become proficient in surgery and to meet the requirements for fellowship in the College and for certification by the specialty boards. Officers, while receiving this training, will be on active duty with pay and emoluments, and they will have the benefit of almost constant association with the chiefs of services on full time duty in the hospitals. Such a program of training will facilitate expansion and reorganization of the Army, Navy and Veterans Administration by attracting temporary officers who are interested primarily in a surgical career.

If history is repeated the Presidential proclamation terminating the national emergency may be delayed as long as two years after the cessation of active military operations which, with the six months thereafter, as provided by existing law, will offer an excellent opportunity for graduate training in the service hospitals over a considerable period of time and will correspondingly ease the training load to be carried by civilian hospitals.

THE PUBLIC INTEREST—MEDICINE'S OPPORTUNITY

The prospects are that the postwar period will bring unprecedented demands for the services of surgical specialists. The first World War gave tremendous impetus to medical and surgical specialization. Today war medicine is again con-

tributing to enhanced appreciation of the value of the surgeon who has exceptional skill in a specific field. Aroused public interest is medicine's opportunity.

Special skills are best developed through systematic educational programs, in selected hospitals, whereby the fundamentals of medicine and surgery are mastered before training is narrowed and concentrated upon the specialty. Appreciation constantly grows of the necessity of understanding the functioning of the body as a whole before success can be expected in treating any part of it. The day is near when hospitals generally will extend privileges to practice a specialty in their institutions only to those who have had the requisite general and special training to insure competence. Many hospitals already limit privileges in this manner, no longer recognizing the physician who elects to practice surgery and the surgeon who elects to practice a surgical specialty without first obtaining the proper training in an approved institution.

The pivotal point in the training program is unquestionably the senior surgeon in the hospital which conducts graduate training in surgery. Upon his conscientious preceptorship the success of any plan will depend. There can be no substitution for the personal interest of the experienced surgeon in the progress of the learner. Hence the ultimate responsibility for the success of postwar graduate training will rest not alone upon hospital administrators and medical associations, but upon the Fellows of the College and other competent surgeons who assume personal responsibility for upholding high standards of training.

Leadership has been wisely exercised by the surgical profession and it is demonstrable that in the critical educational situation which now exists the American College of Surgeons is well prepared by its established program to direct the voluntary efforts of surgeons to apply effective remedies to overcome the losses sustained during the war. The teaching hospital is the essential instrumentality. We shall need many more.

The future of surgery is involved in the preparation for postwar world leadership in the healing arts as now planned and developed by physicians and hospitals in the American countries. The surgeon who helps his hospital to maintain or to inaugurate a program of graduate training in surgery under the wartime difficulties is rendering patriotic, scientific, educational, and humanitarian service, and is helping his profession and his hospital to build a firm foundation for public good will now and after the war.

SURGERY

Gynecology and Obstetrics

An International Journal of Surgery

FRANKLIN H. MARTIN, M.D.

Founder and Managing Editor 1905-1935

Volume 80

JANUARY TO JUNE, 1945

PUBLISHED BY

THE SURGICAL PUBLISHING COMPANY OF CHICAGO

54 EAST ERIE STREET CHICAGO ILLINOIS, U. S. A.

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January, 1945

International Abstract of Surgery

Supplementary to
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INTERNATIONAL ABSTRACT OF SURGERY

VOLUME 80

JANUARY, 1945

NUMBER 1

THE PREPONDERANCE OF GALLSTONES IN WOMEN

An Etiological Study

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IN studies on the occurrence of gallstones one of the few facts on which almost all authors are agreed is that women are more frequently subject to gallstone disease than are men.¹ This conclusion is one of the outstanding features encountered in any review of publications about gallstones. In a recent paper on 'Pregnancy and Gallstones' by Robertson and Dochat statistical data on this subject were recorded and reviewed. Among the patients of the Mayo Clinic women's susceptibility to the formation of gallstones when compared with that of men gave the proportion of 1.8 to 1 and in a combined summary of reports of similar statistics from 22 writers, this proportion was found to be 2.2 to 1. The usual explanation offered to account for this fact was that pregnancy favored the occurrence of gallstones, but the authors just cited after a fairly complete review of this question concluded there was considerable doubt as to the validity of the theory that childbearing could wholly account for the preponderance of gallstones in women. Consequently some other solution appears to be necessary and the present study is presented with that end in view.

A detailed examination of all the theories which have been proposed to explain the presence of gallstones would lead too far afield. However a brief review of the salient elements of these theories may lead toward a more nearly correct orientation with the main problem.

The only notable exception to this statement is found in a paper by Miyake and Ishiyama (1930). They endeavored to prove that the increased tendency toward the production of gallstones among European and American women, as compared with men, was due to their custom of wearing corsets, as the Japanese women, who did not wear corsets, had no higher incidence, they asserted, than did men. However the figures of other Japanese writers do not support this contention.

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tation with the main problem. Such an effort at once encounters the usual difficulties. It is not only confusing but also astonishing to see how much authors diametrically disagree as to the significance of the data they have collected. No single cause (or even multiple causes) has proved to be a satisfactory explanation for the formation of gallstones, although writers have placed varying emphasis on one or more of what they frequently designate as *predisposing influences*. For simplification I have elected to discuss these under the following headings: (1) stasis of bile, (2) changes in the constituents of bile, (3) infection, (4) associated diseases and constitutional susceptibility, and (5) neurogenic disturbances.

STASIS OF BILE

Almost as early as gallstones were recognized the theory was advanced that they were due to the too prolonged retention of bile in the gall bladder. In the middle of the sixteenth century pathological stasis of bile was emphasized by Fernel when he wrote "They [gallstones] come from bile that is held back too long is not emptied or not renewed." Coe, in 1757 asserted stagnation and inspissation of bile, particularly in women accounted for women's greater liability to acquire gallstones. Nearly a century later (1842) Rokittansky concluded that gallstones were the result of stagnation and the holding back of bile. Meckel von Hemsbach (1856) similarly agreed that no gallstones could be formed "if the factor of stagnation was absent." Kraus (1881) stated that an intermediate cause of gallstones was a slowing of the flow of bile into the intestine and a resultant *Anhäufungen* (accumulation) of bile in the gall bladder and Cohnheim (1882) referred gallstones to a difficulty in the emptying of the gall bladder.

Marchand (1888) made the broad generalization that everything which led to thickening of the bile obstruction of the bile ducts or insufficient emptying resulted in granular (koernigen) deposits from which larger concretions might readily be formed. Klebs (1889) asserted that "the preliminary condition [*Vorbedingungen*] for gallstones is stagnation of bile." Naunyn (1891) wrote, "Stasis is the decisive cause of gallstones and Stagnation of the bile remains the only well established cause of the formation of gallstones." Luetkens asserted that Naunyn's most important contribution to the etiology of gallstones was the idea that stasis was a *conditio sine qua non* for gallstones. Other prominent authors, including Welts (1894) Gumprecht (1895) Aschoff and Baumeister (1909) Grube and Graß (1912) Aoyama (1914) and Meltzer (1917) reached similar conclusions. Later writers were equally impressed by the importance of this factor. For example Rous and McMaster (1921) stated, "Intermittent biliary stasis is admittedly the principal predisposing cause of cholelithiasis, while Chaulffard (1922) appeared certain that stasis, no matter what the cause favored changes in solubility due to overconcentration of cholesterol and consequent precipitation." Again in 1924 Rous, Drury and McMaster (1924) wrote that stasis leads "to accumulation of organic debris." Whitaker (1927) was equally emphatic in the statement "The fundamental condition then to gallstone formation is universally recognized to be stasis," and in 1929 (221) under the title Biliary stasis as a factor in the production of gallstones he said "On the whole recent studies confirm the old opinion that stasis is an essential factor in gallstone formation. Again in 1934, Whitaker (222) echoed Fernel in the conclusion, "Any condition in which the bile remains an abnormally long time in the gallbladder predisposes to gallstone formation and finally stated, "Practically all students of the subject have agreed that one factor necessary to gallstone formation is stasis either in the gallbladder or ducts." Westphal (227) in 1922 also asserted that in man stasis without infection or bacteria could lead to precipitation of bilirubin and cholesterol while Schaefer (1932) expressed almost the same opinion when he stated, "The principal factor (in the precipitation of cholesterol) is concentration by absorption of fluid and stasis is the usual cause of this." Finally in a late edition (1938) of Osler's "Text book of Medicine" the statement is made that "all conditions favoring stasis predispose [to gall stones]"

Naturally enough, the conditions which might conceivably produce stasis have received early and repeated consideration. Mechanical factors, such as anatomic peculiarities of the biliary tract, increased intra-abdominal tension (especially during pregnancy) pressure on (or distortion of) the bile ducts by the pregnant uterus, and relaxation of the abdominal walls producing ptosis of viscera² after pregnancy frequently have been mentioned. The theory first proposed by Heidenhain in 1863 namely that the normal respiratory movements of the diaphragm served as an adjunct to the drainage of the biliary system including emptying of the gall bladder and the conclusion that increased abdominal pressure, as in pregnancy interfered with this function, have had many advocates, even as late as 1932 when Blood supported this view. Other careful investigators have failed to confirm these notions.

Klebs in 1872 and Marchand in 1888 called attention to the fact that at postmortem examinations, a transverse groove across the right lobe of the liver was occasionally found. This was noted particularly in women and was called "Schnurleber." It was ascribed to the tightly laced corsets prevalent among women at that time. Several later writers agreed with Marchand that this custom favored the stasis of bile and, thus, the formation of gallstones.³ As tight lacing became less customary this theory was, perforce, abandoned.⁴ In support of other factors assumed to result in biliary stasis, frequent references were made to the alleged sedentary habits of women,⁵ to obesity and to old age.

Some writers, however have minimized the role which stasis might play in the etiology of gallstones. Thus Schade (1910) concluded that, although stasis of bile in the gallbladder was a very important factor in the precipitation of cholesterol from the bile, this precipitated cholesterol was not identical with the formation of calculi, and that other influences seemed to be necessary. A few authors even denied that stasis was of any particular moment. Hein as early as 1846, made the shrewd observation that "Ruhe (rest) alone was not sufficient to produce gallstones, as the bile reg-

²Harrold (1922), as the result of direct observation during abdominal operations, stated, "There was very rarely complicated by ptosis."

³The same deformity of the liver occasionally found in men, was supposed to be caused by tight belts, particularly the sword belts of military men (Manser, 1891), and a similar reference was pronounced to result from the use of the corset (Marchand, 1888).

⁴And yet as Marchand (1888) the following quotation from Meyer (1909) appeared in prominent medical journals: "Any limitation in the flow of bile may result in various gallstone troubles. The year round use of anything tight around the abdomen. A lady wears too tightly around the middle, or girdle that is worn too tight in the worst time because she is."

⁵Osler-Snyder recorded that J. P. Frank, in 1872, noted that obesity and ptosis were supposed to favor gallstones, and Bock, in 1879, noted that literary men, priests, and persons who were sedentary were all prospective subjects for gallstones.

⁶Gumprecht wrote "besides stasis there is no other single cause of gallstones."

larly undergoes short periods of Ruhe during inactivity of the intestine. Sixty-eight years later (1914) Lichtwitz asserted that the idea of stasis as a factor in the production of gallstones was not surely established. Rovsing (1923) noted that Aschoff had accepted stasis as "an irrefutable fact" ("eine unerschütterliche Tatsache") and that from this one would conclude there was a large amount of convincing proof behind it. Unfortunately he added one seeks in vain for any such evidence. Rovsing also noted that acquired obstructing biliary lesions in man did not necessarily produce gallstones. Gundersmann (78) wrote in 1926 "The idea of stasis is entirely hypothetical and said that it would be better to drop completely this uncertain theory." Mentzer (1927) stated that stasis of bile was not essential for gallstone formation and Schmidt (1930) agreed with Gundersmann that the theory of stasis was somewhat hypothetical. Newman was more emphatic when in 1933 he wrote "Stasis in itself is no explanation for anything" he also said "The magic word stasis on analysis disappears from the list of primary causal factors [of gallstones]" while Andrews (1933) adopted this opinion by stating "There is no evidence that stasis alone is a factor." In 1935 Pavel asserted "The theory of the corset, atony of old age and other causes of stasis have failed [to explain gallstones] and added "The history of the corset as a cause of stasis and lithiasis represents a symbol of the role of inertia in the maintenance of old theories. Also in 1936 in the second edition of their book on "La vesicule biliare, Chury and Pavel expressed doubts about the importance of stasis in the production of gallstones as they had frequently observed stasis both experimentally and clinically without finding gallstones. Greene and his coworkers (1936) agreed with Andrews that biliary stasis alone is insufficient to produce calculi. Eppinger (1937) flatly asserted "Stasis alone never leads to cholelithiasis" (Stauung allein führt nie zu Cholelithiasis). In 1939 Carter, Greene and their colleagues reported that they found biliary stasis present to an equal degree in noncalculous and in calculous gall bladders and stated "While there is strong presumption that stasis was of importance in the formation of gallstones, other unknown factors must also have been in operation."² Finally Galland

and Baker in 1940 asserted that neither biliary stasis nor stasis in the pancreas is a single factor producing gallstones.

Summary Although stagnation of any fluid in which precipitation of its elements is to take place would appear to be a necessary requirement this factor does not seem to play an important role in the formation of gallstones. As Hein pointed out in 1846 the bile normally undergoes periods of quiescence. The length of such periods is determined largely by the quality of the ingested food as well as by the normal digestive functions of the upper part of the gastrointestinal tract. Even during the times of active evacuation it is probable that the gall bladder frequently is not completely emptied. During its stay in the gall bladder the bile is concentrated up to about a tenth of its original volume because of active absorption of water and water-soluble salts. This natural quiescence of bile in the gall bladder can hardly be accused of giving rise to gallstones, and repeated observations indicate that abnormal stasis created by such obstructive phenomena as lodgment of a calculus in the cystic duct, or carcinoma or stones in the common bile duct never produces, or even favors, the production of gallstones. Stasis so useful in the laboratory test tube experiment, is not the cause of gallstones.

CHANGES IN BILE

Although there is no evidence that Paracelsus (1493-1541) had any intimate knowledge of gallstones (or of any other pathological condition for that matter) his was the earliest attempt to establish a chemical cause for certain diseases.³ What he denominated as "tartaric processes" was the basis for a doctrine of calcification and concretion formation and was applied by him to all sorts of calcific deposits as well as to calculi. According to Muleur he included sediments in the cavities of the body such as the urinary bladder and the channels of the liver. In his *Opera Paramirum* published in 1572 the following sentence occurs, "Now however the bile contains this same Tartarum and it thus happens that in the bile lies the material for stones." Plater (1536-1614) compared gallstones to stalactites and spoke of a foreign substance which modified the constitution of the bile. Thenard (1821) thought the precipitation of bile pigment came from a diminution of Natron (alkaline salts) and Seifert (1851) inferred that increase of lime in the drinking water was important. However Thudichum (1863) is

¹Ich glaube man setzt drei Ursachen zusammen Begriff ganz fallen zu lassen. (Greene, 1936)

²In their book on changes of the biliary tract, published in 1939, these same authors wrote on page twenty-four, "Calculi have been observed under conditions which seem to preclude the presence of stasis." Two pages farther on, in discussion of the hypertrophic gall bladder, they stated, "The concept of stasis explains many of the clinical features of the disease. First, on page forty-two, they said, 'In patients with typical gall-bladder symptoms, the stone located in the gallbladder, but palpation in the abdomen results of stasis, and the most frequent accompaniment of gallstones in operative specimens.'

³Alfleur (1846) called Paracelsus "the first popularizer of the general pathology of diseases," while Lutz (1923) said he was "the great searchlight of the medical Renaissance."

usually given credit for being the first to express a more rational theory—namely, that fermentation (Gaerung) of bile caused a precipitate by splitting the bile acids and alkalies. The pathologist Klebs, whose views on many phases of disease were far ahead of his time, wrote in his "Allgemeine Pathologie" (1889) that although the presence of gallstones furnishes many perplexities, nevertheless one thing is sure, namely that they arise from a metamorphosis of the normal constituents of the bile.

In 1789 De Fourcroy made known the discovery of cholesterol and asserted that all human gallstones contained this substance. It was given its present name by Chevreul (38, 39) in 1815 and 1816 and in 1821 Thenard assigned to it the principal role in the formation of gallstones. Since then there have been innumerable attempts to determine the conditions which govern the normal and pathological metabolism and the fate of this very important substance, particularly in its relation to bile and gallstones. Both speculations and experiments have been freely employed to explain why it is normally kept in solution in the bile and what circumstances intervene to cause its precipitation. With the identification of bile acids, first about the middle of the nineteenth century the suspicion arose that these acids and their salts were concerned in keeping the cholesterol of the bile in solution. Klebs (1889) expressed this view when he stated: "Cholesterin is held in solution by the bile acid salts and can only be precipitated when these [salts] are diminished." Many others have confirmed this statement, especially Andrews and his colleagues (1932) who demonstrated that by dialysis *in vitro* bile salts will pass through a semipermeable membrane and leave cholesterol deposits behind. Andrews and his associates (1933) further agreed with previous authors that "no substance other than bile salts in the bile is capable of holding cholesterol in solution."

It is suggested by many workers. Some were able to demonstrate a slight increase of cholesterol in the blood in the later months of pregnancy but it was not clearly evident that hypercholesteremia, from any cause, uniformly affected to any important degree the cholesterol content of the bile or what is more important, the production of gallstones. Similarly, feeding experiments gave contradictory results, although it appears probable that a persistently high fat (or high protein) diet increases the amount of biliary cholesterol. All of the experiments and observations in the field represent a sort of groping after the cause of gallstones. Many workers have been convinced that once a consistent increase of cholesterol in the blood or bile from any cause can be demonstrated, that cause would have an important bearing on the production of gallstones. Among others, Carter and his associates (34) and Rehfuess and Nelson advised a diet low in cholesterol as a routine treatment for persons who have, or may have, gallbladder disease. But the increase or decrease of cholesterol in the blood or bile from any cause has assumed relative unimportance as long as the proper ratio (of solubility) between bile salts and cholesterol could be maintained.

In 1927 Herzheimer wrote, "The question of nuclei is the principal problem of gallstones. The well known tendency of some substances in solution particularly crystalloids to agglutinate around some sort of a central core (or nucleus) undoubtedly was responsible for the widely held notion that biliary constituents, especially cholesterol and bile pigments, could precipitate and collect around inert substances. These have been variously described as clumps of bacteria, epithelial and other cellular debris, pigment particles, intrahepatic bile-duct concretions, cholesterol polyps, or masses of mucus. Numerous and largely unsuccessful attempts were made to produce gallstones by implanting foreign bodies in the gall-

Closely associated with the concept of a nucleus is the supposition of some kind of a binding substance. Hippocrates and Galen are said (Weiser and Gray 213) to have recognized this possibility and von Heyde in 1684 extracted the crystal line material from a urinary calculus and observed a residual framework. For many authors, mucus appeared to fulfill the requirements for a central core as well as a cement substance. Kemp of London in 1856 stated "The mucus of the gall bladder is not merely a secretion designed to lubricate the interior of that organ and protect it from irritation by its other contents but it is an essential and integral portion of cystic bile. In that same year Meckel von Hemsbach concluded "Two basic factors underlie the formation of every true gall or urinary stone: first the presence of an organic substance, mucus, in which there may be deposition of salts; second a suitable urinary or bile fluid to serve as the mother liquor for these sediments. The decomposable organic substance, mucus, is unquestionably necessary. Stones are formed only when an organic binder is carried down too. Eighty-four years later (1940) Alvarez expressed a similar conclusion when he wrote "It is well known that the mucous membrane of the gall bladder secretes a small amount of viscid alkaline mucus. This probably causes trouble at times by serving as a cement for the formation of gallstones.

However Aschoff (1905) could not obtain a positive staining reaction for mucus in the mucosa of the normal gall bladder. He thought there might be a special kind of mucin or some "Vorstußen" (antecedent) to mucin. Chiray and Pavel (1936) likewise were puzzled, because they said "One cannot find specifically staining mucus in the bile. They referred to Wahlgren who in 1901 had determined that the cells of the mucosa of the human gall bladder secrete not mucus, a glycoprotein, but a mucinlike material nucleoprotein (or nuclealbumin) which differed from true mucin by the absence of a reducing substance. Wahlgren thought true mucin probably arose in man from the epithelium of the bile ducts as he always found mixtures of true mucin and nuclealbumin in human gall bladders. With this conclusion Hammarsten (1905) who wrote extensively on this subject was in full agreement. But Polcard (1922) stated that while properly speaking there are no true mucus glands in the gall bladder nevertheless its cells can readily take over the function of producing mucus just like the intestinal epithelium. Each cell of the epithelium (of the gall bladder) can secrete (mucus) and does so to a variable extent. Johnson (1922)

maintained, "The epithelial cells of the gallbladder mucosa secrete mucus more abundantly in proportion to the surface than any other [group of] mucus secreting cells. Harding studied the subject in 1934 and agreed with Polcard and also noted a similar opinion by Jurisch in 1910. Harding claimed to have found in the epithelial cells of normal gall bladders mucous granules which stained well with mucicarmine. Finally Ivy (1934) in a review of the physiology of the gall bladder said, "The gallbladder secretes a viscid colorless secretion its viscosity being due to protein rather than to true mucin, which if present, is only in traces.

Aschoff in 1906 and in 1913 referred to what he and others including Flandin (1912) called the Erweisskelette or Erweisgeruest (albuminous framework) of gallstones, which Kuru who worked under Aschoff concluded was fibrin. This albuminous substance was presumed to enter the bile either in the form of an inflammatory exudate or as an abnormal product of injured liver cells, and to produce albuminocholia, which was emphasized by Lichtwitz (125) as comparable in some respects to the albuminuria of pregnancy.

In the fifth edition of Wells' "Chemical Pathology" are found the following broad generalizations. All pathological concretions appear to be laid down according to a definite law. There must first be a nucleus of some substance different from the substance that is to be deposited and which is most frequently a mass of desquamated cells but may consist of clumped bacteria, masses of mucus precipitated protein or a foreign body of almost any sort. Upon this nucleus, substances crystallize out of a solution much as cane sugar crystallizes on a string to form rock candy but with the important exception that among the crystals is usually deposited more or less mucin or other organic substance which forms a framework in which the crystals lie and which remains if the crystals are dissolved out as a more or less perfect skeleton of the concretion. In no case would the concretion form were it not that the solution is overcharged with some substance but not infrequently it is the presence of the nucleus that leads to the precipitation of the substance that is the nucleus may play either a primary or a secondary role. With a few exceptions the dissolved substance is deposited in a crystalline form, although the crystalline structure may in time partly disappear through condensation or through filling the interstices with some other material. The structure of the concretion depends on two factors. The crystals tend to be deposited at right angles to the surface and thus give a radiating structure

The ease and frequency with which the presence of *escherichia coli* was demonstrated in the bile together with the evidence that cholesterol could be precipitated in vitro from bile inoculated with these bacteria (Gerard 1905 Kramer 1907 de Lavergne and Kiesel 1935 and many others) proved a very seductive and reasonable theory to explain the cause of gallstones.

However several writers, especially Rovsing disputed the validity of this conclusion. Gumprecht (1895) asserted that the normal bile is free from micro-organisms and that the notion that gallstones are formed from symptomless infection of the bile was "nothing but an hypothesis." Chauffard (1922) observed that for some physicians and surgeons the infectious origin of biliary lithiasis is a kind of dogma and concluded that the largest number of gall stones escape an infectious pathogenesis." Lichtwitz (1929) called attention to the fact that severe purulent biliary infections render certain no gall stones will be formed (Schwereltrige Gallenprozesse machen sicher keine Steinbildung).

A similar story could be related about the rise and fall of the theory that *ebertella typhosa* caused gallstones. The former world-wide epidemic of typhoid fever and the frequently proved presence of *ebertella typhosa* in bile and also in gallstones, as well as in the walls of gall bladders of typhoid carriers, served to indict this organism by testimony similar to that used against *escherichia coli*. But when the incidence of typhoid fever greatly declined and the incidence of gall stones remained the same or showed an increase, this explanation of their cause had to be abandoned.

In more recent times, little convincing evidence has been presented to prove the primary importance of the infectious theory although for many writers, the dicta of Naunyn (150) and his school still prevail. In 1924, Schragr suggested that the gall stones of middle life are the end product of a cholecystitis which originated during the first pregnancy. Branch (1929) added to the confusion by asserting that "the organism recovered from a case of acute cholecystitis is not necessarily the primary etiologic factor responsible for the development of the acute lesion. Umber (1932) concluded that the presence of bacteria in the bile (bacteriocolia) did not necessarily mean disease, as the lower part of the biliary tract always contained micro-organisms. He also mentioned that an otherwise harmless organism might become pathogenic. Even as late as 1932 Aschoff (12) apparently was much impressed by the data concerning the association of the enterococcus with

infection of the biliary tract.¹ The accumulated literature on the relation of bacteria to the production of gallstones, as well as to other diseases of the biliary tract, has grown to enormous proportions. Every conceivable aspect has been investigated. The kinds of micro-organisms, their paths of entry into the bile, the nature of the lesion they produce the attempted simulation of these activities by experiments with laboratory animals, and many other phases of the subject have received attention. However clear-cut proof that gallstones are ever primarily caused by infection with bacteria has not yet been offered. Carter and his coworkers (1939) adopted a somewhat cautious view when they wrote, "As the result of many careful pathological, bacteriological and physiological investigations we are coming to the conclusion that infection is the primary cause of disorders of the gallbladder in the minority of cases, and they finally summed up the matter by the following statement. Experiments pertaining to the origin path and effects of infection upon the gallbladder have been conducted by Roseow, Graham, Judd, Mentzer (142) MacNeal and many others without arriving at final conclusions as to the specific role played in gallbladder disease by infectious bacteria.

Summary On the whole there is little evidence in favor of the theory of infection. At the same time both the occurrence and the seriousness of infection of the biliary system by virulent bacteria must be admitted. They may cause profound and often fatal disturbances. Also, micro-organisms, of all degrees of pathogenicity including purely saprophytic types, may and undoubtedly do gain entrance to the bile and are occasionally demonstrable in that medium, in the walls of the gallbladder and even in the gallstones themselves. Theoretically they may, by agglutination, form clumps which act as nuclei for the aggregation of precipitated cholesterol and bile pigments. However, the theory that they play any major role in causing gallstones must be abandoned.

ASSOCIATED DISEASES AND CONSTITUTIONAL SUSCEPTIBILITY

In the efforts to detect some common basis for the formation of biliary calculi, repeated studies have been made of the possible etiological relationship of gallstones to other diseases. The earliest of these was undertaken to prove the simultaneous occurrence of urinary calculi and cholelithi-

¹This organism was named by Tiberius in 1890, and in 1902 was called the "bacteriocolia" by Anderson and Herber. Its chief claim to recognition arose from its apparently frequent presence in the bile (Meyer 1904; Meyer and Lippman, 1905, and Pomeroy, 1911), as well as its resemblance to *escherichia coli* in shape and ability to ferment in bile.

asis. However the number of patients who harbored both types of stones has not proved to be large enough to justify any thought that they had the same cause. For one thing more men than women have urinary calculi, while the reverse is true for gallstones. The relative incidence of other diseases, such as arteriosclerosis, gout, and even fatty changes in the liver and tuberculosis, in cases of gallstones has been reviewed with the same end in view but with not even suggestive results.

The statement that there is an increased incidence of gallstones in cases of diabetes seems to have good statistical support. Isolated instances of diabetes or glycosuria developing after attacks of gallstone colic, often with jaundice have been reported by several early writers. Loeb apparently was the first to report such a case in 1879 and other cases have been reported by Hull (1882) Kraus (1884) Roger (1886) Ord (1887) Sweet (1889), Gans (1891) Gilbert and Well (1898) Weldenbaum (1898) and Kausch (1899). In answer to a discussion of his paper by Gans, Naunyn (190) expressed doubt as to any association of gallstone colic with glycosuria, and in his book (191) published in 1892, he stated 'I cannot confirm from my own experience the frequent appearance of sugar in the urine in connection with gallstone colic. Finally in an article entitled *Diabetes mellitus*, published in Nothnagel's *Encyclopaedia of Medicine* in 1898 Naunyn asserted that in 250 patients with gallstone colic he had not once noted glycosuria except in cases in which the disease was complicated by disease of the liver. Lenné (1898) expressed a similar view. Zinn (1898) held that sugar in the urine of patients with gallbladder disease was a very rare event, and Kausch (1899) concluded 'In gallstone disease (without complicating disease of the liver) glycosuria is very uncommon (*höchst selten*)'. Hochhaus reached a similar conclusion in 1907.

According to von Noorden and Isaac (1927) Bouchard in 1891 was one of the first to report on a series of cases of diabetes. He found gallstones in 10 per cent of his patients with diabetes. Seckel (1925) among 430 cases of diabetes could discover only 26 (6 per cent) patients who had gallstones. Jones and his associates (1925) examined the duodenal contents of 68 diabetic patients and concluded that 15 (22 per cent) of the patients had or had had gallstones. They indicated that 'the existing figure for the incidence of gallstones in diabetics is far too low' and that probably one-fifth of all diabetic patients over forty have an associated cholelithiasis. Wilder in 1926 found that gallstones were present in 16 or 28 per cent, of 58 cases of diabetes in which

postmortem examination was performed at the Mayo Clinic. He believed that disease of the gallbladder is an etiologic factor of importance in diabetes. Woehrmann (1928) found that 160 of 677 diabetic patients had gall-bladder disease and Katsch (1928) reported 'gall-bladder changes' in 14 of his 36 cases of diabetes, an incidence of nearly 39 per cent. Warren (1938) collected data from the records of 453 postmortem examinations of diabetic patients more than thirty years of age. Gallstones were (or had been) present in 140 (31 per cent) whereas in 500 consecutive postmortem examinations of nondiabetic patients of the same age group gallstones were found in only 21 per cent. In 1941 Dry and Tessmer reported that gallstones were present or had been removed by operation in 50 or 27 per cent, of 182 cases of diabetes observed at the Mayo Clinic.

I have reviewed the statistics of postmortem examinations made at the Mayo Clinic during the years 1934 to 1943 inclusive. In 4,761 cases in which such an examination was performed on patients twenty years or more of age sufficient data were recorded regarding the presence or absence of gallstones at the examination or their previous removal by operation. This number 4,761 included 3,016 (63 per cent) men and 1,745 (37 per cent) women. Gallstones were present or had been present in 1,032 cases (22 per cent).¹

Of the 1,032 patients in whom gallstones were or had been present, 500 were men (17 per cent of the 3,016 men examined) and 532 were women (30 per cent of the 1,745 women examined). Diabetes had been diagnosed in 205 of the 4,761 individuals. Of these 205 patients with diabetes 124 were men and 81 women. Of the patients who had diabetes, 76 (37 per cent) had gallstones. Of the men who had diabetes, 41 (33 per cent) had gallstones the corresponding figure for women was 35 (43 per cent). Of the 4,556 patients in whom diabetes was not present and whose bodies were given postmortem examinations, 2,892 were men and 1,664 were women. Of these nondiabetic patients 956 (21 per cent) had gallstones. Of the nondiabetic men 459 (16 per cent) had gallstones the corresponding figure for women was 497 (30 per cent). Thus the presence of diabetes apparently increased the incidence of gallstones in this series by 17 per cent for men by 13 per cent for women and by 16 per cent for both sexes.

Not all authors have agreed that there is any significant relationship between diabetes and cholelithiasis. In 1892 Naunyn (191) stated, 'It is

¹Doehat and I reported the incidence of gallstones at postmortem examinations as 16 per cent in the years 01 to 04, inclusive (1 the Mayo Clinic). We considered all ages, and in many of the earlier records data on gallstones were substantially incomplete.

not permissible to conclude there is a causal relationship seeing that both diseases cholelithiasis and diabetes, are quite common and no special explanation is required of their occasionally attacking the same individual. Strauss (1898) likewise asserted that gallstones never or very rarely are associated with diabetes, and Lenné (1898) agreed that liver diseases and diabetes mellitus do not possess a causal relationship (*Leberleiden und Diabetes mellitus nicht in einem Causalverhaeltnisse stehen*). In 1924, Campbell wrote "There is an equally large amount of cholesterol in the blood in cases of diabetes and some types of nephritis and there is no tendency for gallstones to be associated with these diseases. Fowweather and Colinson (1927) concluded "Increase of blood cholesterol alone does not cause gallstones as it is well known to increase in diabetes but there is no particular relation of diabetes to gallstones. Joslin and his associates (1935) in 1940 noted that Dublin and his colleagues (1934) also were able to demonstrate little or no connection between gall bladder disease and the development of diabetes.

In spite of these and other similar statements it is quite clear and must be admitted that diabetic patients especially women are predisposed to harbor gallstones. Also there seems to be little if any dispute as to which of these two diseases appears first. Joslin and his collaborators (1940) stated that the average age of 189 patients at the time a diagnosis of gallstones was made was forty-seven and seven-tenths years, and in 199 cases of diabetes the average age was fifty-one and three-tenths years. They also quoted Jordan's conclusion that in the average case a diagnosis of gallstones was made twelve and nine-tenths years prior to the onset of diabetes. As to etiological sequence, I have been unable to find a single author who supported the possibility that diabetes favors the formation of gallstones. On the contrary many have contended that patients with gallstones are particularly liable to have diabetes and thereby have inferred that gallstones might cause diabetes. Joslin (1927) suggested that "the gallstone variety" of diabetes was the most favorable type of this disease and that it frequently could be improved or if the diabetes had not yet occurred it could be prevented by the removal of the gallstones. Jones, McKittrick, and Root (1925) Geddes (1926) and McKittrick and Root (1928) agreed¹

Whether the same factors that produce gallstones also may cause diabetes or whether it is only the complications of gallstones, such as infection or injury to the liver that are effective, are matters for further investigation. In either instance the study of the relationship between these two diseases does not appear to furnish any demonstrable clue as to why gallstones are formed.

Frequently final conclusions as to the cause of cholelithiasis have been expressed by such vague terms as disordered metabolism or "metabolic disturbances." These and similar phrases, which are comprehensive and indefinite are often the last resort of the befuddled investigator. Occasionally more exact terminology is employed, as, for example, faulty metabolism of cholesterol, bile pigments or calcium, and hypercholesteremia. But the most commonly used and least frequently interpreted disturbance of metabolism is conveyed by the word obesity. The alliterative phrase, "fair fat and forty"² has become a sort of shorthand among clinicians as a description of those most likely to have gallstone disease. Strangely enough the association of obesity and gallstones has been the subject of very few definite investigations.

In an analysis of 255 patients with gallstones Zellweger in 1913 found that 87 (34 per cent) were well nourished and 14 (5 per cent) were obese. Mentzer (1926) indicated that the percentage incidence of gallstones increased materially with the increase in overweight.

In 1929 Gross reported that the average weight of 143 men with gallstones was 131.65 pounds, and that of 174 women with gallstones was 126.07 pounds, while the average weight of 500 men without gallstones was 119.24 pounds and that of 500 women without gallstones was 103.35 pounds. In an analysis of insurance statistics, Dublin and his colleagues (1934) stated "The susceptibility of fat women to gallbladder disease is evidenced by the high proportion of women, nearly eighty per cent, in this group. They estimated that in their series, 51.8 per cent of the women were at least 5 per cent, and that 22.8 per cent were 15 per cent, above normal average weight. In their book "Diagnosis and Management of Diseases of the Biliary Tract," published in 1939, Carter and his collaborators gave the summary of a sequence suggested by many investigators of gallstones during the past one hundred or more years. In a discussion of the hypotonic gallbladder they stated

Sedentary habits obesity deficient muscular

¹This phrase has been ascribed to Deaver (22) and he actually used it in a paper published in 1920. It was probably employed earlier and perhaps by other authors.

²In justice to Joslin and his colleagues (1935), it is only fair to quote the following quotation from their book: "The treatment of diabetes mellitus, published in 1935. In view of the present emphasis of the common hereditary basis of diabetes we believe that one can no longer ascribe to gallbladder disease primary etiologic role. It seems fair to conclude that although gallstones and cholecystitis occur more frequently in diabetes than in non-diabetics, gallbladder disease cannot be regarded as primary factor in the causation of diabetes.

tone, and low metabolic rates are common in both sexes having this type of dysfunction. Most of the patients belong to the fair fat and forty' group. Joslin and his coworkers (1940) who have emphasized the role of obesity in diabetes stated that they were inclined to agree with Terbruggen (1937) who asserted that the occurrence of gall-bladder disease in a diabetic patient is explained by the obesity which is commonly present in such a person.

In an analysis of the 1032 instances of gallstones previously mentioned (page 7) I found that 578 (56 per cent) of these occurred in individuals estimated to be of normal or subnormal weight. The remaining 454 (44 per cent) were judged to be above normal weight. In the first group (578) there were 333 (58 per cent) males and 245 (42 per cent) females. In the group above normal weight (454) there were 167 (37 per cent) males and 287 (63 per cent) females. These estimations admittedly are not exact. Indeed most figures on obesity can only be approximate. However these figures tend to confirm the opinions of other authors namely that women at least, who have gallstones are inclined to be overweight at the time of their death.

In spite of these figures and the opinions just cited no one has been found who has contended that obesity was a *sine qua non* for the production of gallstones. Bettman and Tannenbaum in a study of gall-bladder disease published in 1944, said, "We purposely chose this woman of thirty-five years of age with black hair and loss of weight to emphasize the fact that the well-known line about fair fat and forty' should not mislead us. Also it must never be forgotten that the gallstone carrier most probably becomes a patient a considerable time after the calculi have formed. More careful study is indicated to determine whether obesity is really one of the factors in the production of gallstones, how obesity influences this production and whether the presence of gallstones tends to promote obesity and even perhaps the sedentary life commonly ascribed to patients, especially women, with gallstones."

Any discussion of obesity and its relation to gallstones naturally introduces the problem of individual and class, or group susceptibility to one or both conditions. Almost from the time that theories about the cause of gallstones began to appear it has been the assumption of many authors that gallstones represent the results of an abnormal constitutional make-up. As Dieulafoy (48) (quoted by Chauffard, 1922) expressed it "L'état diathésique domine le pathogène de la lithiasis biliaire (the diathetic state dominates the patho-

genesis of biliary lithiasis). Other equally vague terms have been employed, such as cholesterol diathesis, constitutional factor 'familial tendency', 'predisposition', "pregnancy cholesterol diathesis", "racial differences," and so forth. Bowen and his associates (1928) were no more specific when they stated that the frequent association of diabetes obesity and gallstones was probably a matter of constitution."

This is not the place to review the literature which has been collected about the relation of constitution to disease.² Attention must be confined to a few pertinent references to the relationship between the production of gallstones and specific body types. One of the earlier authors to hint at this association was Beneke (16) who in 1876 found that of 30 persons with gallstones 19 (63 per cent) had "Eine starke Fettbildung" (a marked corpulence).³ Zellweger (1913) said she had observed an heredity in cholelithiasis in the form of whole gallstone families. Just as in many obscure causes of disease also in cholelithiasis, disposition and constitution play a role. She quoted Bartel, who made the first important studies on this phase of the etiology of gallstones and said "As to the tendency to concretion formation in the front rank is cholelithiasis which frequently discloses an abnormal constitutional predisposition. In 1916 Bartel wrote a paper on "Cholelithiasis und Körperkonstitution" in which he again concluded "In calculus formation, especially in cholelithiasis abnormal constitutional conditions of the entire organism are present. He recommended that in every case in which gallstones are discovered at postmortem examination the constitutional characteristics of the individual should be carefully investigated."

In this country Draper has contributed numerous studies of the relation of physical conformation to specific conditions, especially duodenal ulcer and diseases of the gall bladder. His latest book (49) published with the collaboration of Dupertuis and Caughey, in 1944 is entitled "Human constitution in clinical medicine. These

²In the second edition of Dieulafoy's "A text-book of medicine" (47) translated by Collins and Liebsmann and published in 1912, the following sentence appears: "My ideas agree absolutely with those expressed by Huxley—that the diathesis is a factor in the pathogenesis of lithiasis." Dieulafoy also summarized the theory which then prevailed in France when he stated, "Biliary lithiasis is often associated with the diathetic conditions that form part of the group of arthritic diseases—rheumatism or rheumatism, urinary lithiasis, obesity, asthma, diabetes and eczema." The word "arthritic" is used in the sense of the French word "arthritisme" (arthritic diathesis) which was employed by the writers of Dieulafoy's time with broad and special significances.

³The subject has its own journal (Zeitschrift fuer Leber- und Gallenkrankheiten) and references to it have reached astronomical proportions. Tucker and Lewis in 1920 estimated that, in the previous five years, fully 7000 titles had been listed.

⁴According to Fegeshbaum and Howitz (154) Brodie (17) in his book entitled "Die Atterdisposition," published in 1870, was the first to report measurements of the body in support of his theory.

authors reported studies on 90 patients with diseases of the gall bladder. After noting that "women are more prone to gallstones than men in the proportion of five or six to one, and recalling the old medical saying that the commonest type of woman to be affected is fair fat and forty" they concluded from numerous physical measurements and observations that, when gallstones occur in man there is a "strong emphasis on gynecic characters in his total person. These included 'gynecic contour, fat distribution, gesture, facial expression and turn of mind.' Men of gallbladder type possess wide heads, moderately short and broad faces. Roundness and softness characterize the otherwise regular features of the face and their hips are somewhat broad and the trunk is rather short. The massiveness of the gallbladder physique is more clearly shown by the very broad and deep chests which exhibit the largest circumference found in any male group. Similarly these authors asserted that 'women with gallbladder disease are in general of a soft, round or lateral type of build. These women the authors claimed, have 'fairly broad shoulders and the broadest hips of any female disease group. Their chests are by far the broadest and deepest and the chest circumference-stature ratio is the largest recorded in the study."

Disagreement is usual with every theory about the pathogenesis of gallstones (or any other disease for that matter) and some authors do not admit the influence of constitutional tendencies in this disease. Chauffard in a masterly book on biliary lithiasis, published in 1922 rather naively concluded that, on the whole, heredity played no important role, but in men in whom hypercholesteremia (which was observed by him in women during pregnancy) was not present "heredity is more important." Feigenbaum and Howat (1934) reported as follows "Our results do not bear out Draper's conclusions. In 1935 they asserted "The conception that the physical constitution of a person is an important factor in the etiology of disease arose from the observations of the effects of certain diseases on the body. At no time were these effects controlled in investigating the subject. Thus a clinical impression which is erroneous, viz. that the anatomical habitus is one of the causes of disease, was perpetuated." Tucker and Leasa in a lengthy review entitled 'Man a constitutional investigation' (1940) commented as follows "Draper presents a mass of statistical data which is exceedingly hard to evaluate."

Finally Julius Bauer the dean of modern writers on constitution and disease in 1912 wrote as follows in reference to Draper's theory: "The etiology and pathogenesis of most diseases are too complicated to conform to so simple a concept as that mentioned. One can hardly expect an ulcer or gallbladder type of human habitus. What may be and has actually been found however is a greater frequency of various diseases in persons exhibiting a particular habitus. Habitus is never the cause of a disease. It may be an indicator of a morbid disposition. Thus one must leave this fascinating question. I have an idea that the last word along these lines has not yet been written, but concerning the theory that constitutional factors play any effective part in the primary pathogenesis of gallstones, there seems to be considerable doubt."

Summary The attempts to associate in causal relationship any other disease and cholelithiasis have proved uniformly unsuccessful. Apparently more diabetic patients have gallstones than do nondiabetic patients and there must be some, as yet hidden explanation for this fact. Almost all investigators are agreed that diabetes, when it occurs, follows the presence of gallstones, but none has proposed that diabetes causes them to form or that the two diseases have a common cause.

In regard to obesity and gallstones, the inquirer finds much confusion in attempts to correlate the two conditions. Most of this arises from the uncertainty as to the actual time at which biliary calculi begin to form. It is the status of the individual *before* this time and not afterward that is pertinent, and for this period of life there is naturally little or no information obtainable. The problem of overweight is closely linked with the effect, if any, of heredity and constitutional tendencies. Here also it is difficult to trace any simple or understandable relationship. The proponents of specific constitutional patterns for given diseases have not produced, and perhaps are not concerned with etiological data. However they have gathered together an imposing array of scientific collaborators and have presented so many facts that their claims cannot be ignored. It seems eminently reasonable that certain types of individuals who possess, largely by inheritance, similar physical structures and mental traits should thereby be subject to similar pathological conditions. Mental hospitals are filled with examples of this tendency. The physically awkward and careless thinking person is a poor risk for accident insurance. But even if the individuals who are going to acquire gallstones could be selected on the basis of their build and disposition, at present one is no nearer

Dubin and others (1931) reported that Draper "went so far as to say that he could go down the side of a corpse in hospital and pick his gallstone cases."

to a solution of why they or the many others who do not conform to this type have gallstones

NEUROGENIC DYSFUNCTION

In all the welter of theories and etiological data, it was inevitable that neurogenic phases should receive consideration. In the early part of the eighteenth century Hoffmann (1731) according to Luetkens stated that the nerve anastomoses between the stomach and duodenum on the one hand and the bile ducts on the other could lead to 'irritative Irradationen'. In the more than two hundred years since then similar concepts frequently have been expressed. The possible association of duodenal ulcer or even disease of the appendix with gallstones has been thoroughly explored. In 1930 Birch and Boyden suggested that the dysfunction and stasis of the gallbladder [with the consequent formation of gallstones] may be due in part to inhibitory reflexes arising from chronically diseased portions of the gastrointestinal tract.

The temptation to review all the stages in the development of the so-called neurogenic theory must be resisted. It should suffice here to note that, preceded by the ideas of John Berg among others, and encouraged by his chief von Bergmann Karl Westphal in 1922 published a 'mile stone' paper entitled 'Relation between the pathology of the biliary tract and the vegetative nervous system'. Other communications by Westphal followed on various phases of physiological, especially neurogenic, as well as pathological and clinical manifestations of the activities of the biliary system. In 1931 Westphal and his colleagues (219) published a book entitled 'Gallenwegsfunktion und Gallensteinleiden' (Biliary tract function and gallstone disease). In the following year (218) Westphal brought out a review of his previous ten years work on 'The motility and absorption disturbances of the bile ducts and their complications'. He noted that since the report of Nauyn (151) stasis in the biliary tract had been regarded as a prerequisite for the production of gallstones and that he (Westphal) had demonstrated that this stasis was the result of a 'dyskinesie' of the musculature of the extrahepatic biliary system. As proof of his theory he referred to the results of previous experiments on rabbits, in which by means of a weak irritation of the vagus, he claimed to have noted an increase in the motility of the smooth muscles of the gall bladder and bile ducts, with consequent contraction of the gall bladder and expulsion of bile into

the duodenum. If the stimulation of the vagus was stronger there resulted a spastic contraction of the ring muscle of the papilla of Vater together with increased tonicity and contraction of the muscle of the gall bladder. But the flow of bile into the intestine was prevented by the spasm at the entrance of the duct into the duodenum. This effect he denominated 'hypertonic biliary stasis.' The opposite of this was caused by stimulation of the splanchnic or sympathetic nerves, which caused relaxation of the musculature of the biliary tract with passive dilatation of the gall bladder a 'hypotonic biliary stasis'. Westphal concluded from these and other observations that overstimulation or oversensitivity with resulting abnormally strong responses of either the sympathetic or vagus (parasympathetic) nerves produces a pathological disturbance in the physiology of the biliary system and prevents the prompt discharge of bile and thus tends to favor infection gallstone formation bile-duct colic and other clinical manifestations. He called the nervous dysfunctional state a cholangiopathy and asserted that it occurred more frequently in women because they were more liable to hypophyseal or gonadal hormonal disturbances, particularly at menstrual periods or because of pregnancy. He affirmed that in pregnancy the evidence of a hypertonic gall bladder stasis with slowing of the emptying time, which had been demonstrated by pharmacologic experiments was positively confirmed by the use of special dyes and roentgen rays. He interpreted these phenomena as signifying an increased sensitivity of the parasympathetic nervous system in pregnancy.

Inhibition of the function of the gall bladder during pregnancy was first demonstrated in animals by Mann and Higgins in 1927. Potter examined the gall bladders during 390 cesarean sections on women at full term. In 75 per cent of these women he found a large distended gall bladder which he interpreted as the result of stasis from some "metabolic dysfunction associated with functional motor disturbance rather than infection or mechanical pressure. Similarly Gerdes and Boyden concluded that there was in pregnant women a hypertonic condition of the common duct sphincter due to a physiologic dyskinesia reflecting the changed hormonal content of the organism in pregnancy. They thought that the stasis of pregnancy sets the stage for the sequence of events which results in the greater incidence of gall stones among women who have borne child.

Earlier 'distensions' in the study of cholelithiasis might be selected as follows: Ferrel (354), Farncombe-Dufresne (185), Merkel von Harnbach (189), Nauyn (189) and Aucher and Barthelemy (190).

Schmiedeknecht and Neuen (1933) called this "cholepathia spastica". Newman (1933), "spastic distention"; Ivy and Sawaburo (1931), "biliary dyskinesia". Lyle Bert and Hicken (1931) used the term "biliary dysmyotonia".

dren From cholecystographic studies many workers reached similar conclusions although there were a few who obtained contradictory results.

Summary. The enthusiasm which has greeted the theories of Westphal and his successors is almost as contagious and far reaching as that which earlier followed the proposal of the infectious theory by Naunyn and his school. It is quite possible that this enthusiasm has led to unjustifiable and too sweeping conclusions, but the mass of evidence that has been collected and the number of previously unexplained phenomena which have now become reasonably and clearly elucidated warrants the expectation that in neurogenic disturbances lies the clue to some of the conditions which govern the formation of gallstones. The transfer of a consideration of purely anatomic changes to a study of purely functional disabilities is a distinct step in advancement of knowledge concerning many diseases including cholelithiasis.

Many other suggestions have been offered to explain the formation of gallstones, chiefly involving minor modifications of the five cardinal theories just discussed but none has received any general acceptance and the defeatist conclusion often has been expressed that multiple and frequently variable factors including some that are still unknown unite to produce gallstones. Thus there has resulted an impasse of sorts on the etiology of gallstones, and many writers have unwittingly agreed with Johannis Schenkii (reference from Chiray and Pavel, 1936) who in 1644 wrote that gallstones, acting secretly make us to be ignorant of the cause. "After a lapse of more than two hundred and fifty years, Rambert in 1899 agreed that 'the pathogenesis [of gallstones] is not clearly known,' and Levyn was equally discouraging when in writing about the gall bladder he said "Even today [1932] there is much about that simple organ that is baffling." Bacmeister was quoted by Kehr (1923) as having concluded "The gallstone is a symptom of a condition in which the diseased picture is not fully revealed nor the special cause of the illness encountered." Salkowski (1922) rather sarcastically remarked that he could not understand why the question of the formation of gallstones produced so much "Kopfschmerz" (headache) among pathologists and clinicians as he was convinced that too much cholesterol or too little bile acids certainly caused the precipitation of the solids of gallstones. Nevertheless he found the problem of why this change occurred a "nicht so leicht zu lösende Frage" (a question not so easy to solve). Roux and others (1919) pessimistically asserted in 1924 "The literature [on the formation of gallstones] has been from early times too heavy

with hypothesis and dismal with uncorrelated observations. A similar conclusion was expressed by Sobotka in 1937 when he said "The formation of gallstones, the role of bile in the emulsification and resorption of fat, the emptying mechanism of the gallbladder are topics, where the extensiveness of the literature is more imposing than its depth and where abundance rather than scarcity of detail detracts from the clarity of the evidence available." After a very complete review of the subject, Laetkens (1936) admitted that although the supposition of Westphal namely that primary stasis of bile is the consequence of motility nervous of the biliary tract, had been confirmed, "the last word has not yet been said on the colloid chemistry or the sources and conditions of gallstone precipitation. Peel (1927) was certain that changes resulting from inflammation of the gall bladder were not fully understood while Sweet (1927) was convinced that "the problem of the formation of gallstones is not a problem merely of infection or of bile stasis, but one involving the metabolism of cholesterol, concerning which we as yet know nothing." In 1929, Lichtwitz (1926) in a paper on the "Principles of concretum formation" asserted that the preponderance of gallstones in women over those in men depends upon drastic anatomic and functional differences between the two sexes, but that it could also arise from some other and unknown cause. He added that although the theories of Berg and Westphal were of great significance there was no proof that they were any explanation for the occurrence of gallstones. "One must conclude," he said, "that the real factor is not known. It may be functional. Nuboer (1931) studied the extrahepatic biliary system and reported "In spite of numerous important researches, the results are inconsequential and as yet only a few definite facts are known on the contrary there are innumerable theories which in general differ widely from each other.

Weiser and Gray (1934) concluded "The precipitation of cholesterin in the gallbladder is altogether inadequate to account for the formation of pure cholesterol concretions." Phemister, Aronson and Peplinsky (1939) asserted that "the fundamental cause of gallstones is very little understood and, finally, Walters and Snell in their book "Diseases of the Gallbladder and Bile ducts" (1940) wrote, "Neither infection stasis nor metabolic disturbances furnish a completely satisfactory explanation of the development of cholecytic disease in general.

In spite of these pessimistic conclusions and in spite of the extremely confusing and often dan-

metrically opposed theories and conflicting results of experiments and observations by scientists during more than four hundred years, several indisputable facts have emerged.

The first and, unquestionably, the most important of these facts is that while gallstones are found in both men and women they occur more frequently in women. It should be emphasized however that, although there is practically universal agreement concerning the preponderance of gallstones in women, this preponderance is not nearly as great as many earlier authors had believed.

In the attempt to explain this well authenticated difference in the incidence of gallstones in men and women, it was to be expected that the functional processes peculiar to women should be closely scrutinized. Therefore, when Schroeder a pupil of Naunyn's in 1892 announced that of 110 women in whom gallstones were found at post mortem examination 99 or 90 per cent, had borne children the problem seemed to have been solved. Most subsequent writers agreed with Naunyn that pregnancy and pregnancy alone accounted for the increased incidence of gallstones in women and there were published numerous statistical surveys which apparently fully supported this contention. In the study by Dochat and me referred to previously there were recorded figures from the reports of 26 authors which showed that of 14,016 women with gallstones, 11,154 (80 per cent) had been mothers. Of 1,413 women who were proved at postmortem examination at the Mayo Clinic to have had gallstones, 1,185 (84 per cent) had had one or more children. Thus the decisive influence of pregnancy as a factor in the formation of gallstones would appear to have been abundantly demonstrated.

But a few writers, notably Branon Scheel Hansen Molnar Hurst, Lichtwitz (124) Gross, and Blumel challenged the validity of this conclusion and Dochat and I made an extensive review of the matter. It was quite evident to us that, as Hurst, among others, had emphasized many authors had completely disregarded the fact that about 80 per cent of all adult women have borne children; therefore, any analysis of the number of adult women with gallstones (or with many other diseases for that matter) would reveal that about 80 per cent of these women also had passed through one or more pregnancies. Thus the view that pregnancy alone accounts for the relatively increased frequency of gallstones in women is largely invalidated. The word, 'largely,' is used advisedly. Although there can be little doubt that pregnancy does not wholly explain why more

women than men have gallstones there is still evidence that pregnancy among other factors may exert some influence in producing this disease. The slight discrepancy noted by several authors, between the percentage of women who have had children and the percentage of those women who have gallstones would tend to support this suspicion.¹

As would also be expected other phases of women's sex functions have received deserved attention. For example Chauffard in 1922 noted a publication by G. P. Gonalous in Buenos Aires in 1916 in which there was demonstrated an increase of cholesterol in the blood of women at each menstrual period. From this and other work, Chauffard concluded that 'during her entire sex life a woman has repeated increases of cholesterol in the blood and this accounts for her predisposition to gallstones.' Okey and Stewart and according to Carter and his colleagues (1939), also Leuret and Dutrent found hypercholesteremia associated with the menstrual periods. Eckelt (1917) called attention to the work of Heilig (1924) who found signs of functional disturbances of the liver during menstruation. Eckelt argued that during the menses the vegetative nervous system is in a state of increased excitability and agreed with Westphal concerning a 'vagotonic motility nervous of the gallbladder' in the menstrual period. Chiray and Pavel (1936) stated that biliary lithiasis is often due to an endocrine dysfunction and directed attention to the irregularity of the menses in such patients.

The disturbances which often accompany or follow the menopause in women have occasionally been cited as factors in causing gallstones but evidence for this view is entirely lacking. That so-called gallstone attacks may and do occur at this period of a woman's life and even that this cessation of function may in some unknown manner favor these attacks cannot be successfully denied. But gallstone attacks must not be mistaken for signs that gallstones are formed at these times.

The last sentence naturally introduces the second fact about gallstones one which in all its phases has certainly not received the attention it

¹The difficulty of determining, by statistical compilation, just how effectively the influence of pregnancy operates arises from the fact that accurate estimation of the percentage of women who have borne pregnant is hedged about by numerous obstacles. Secret abortions and miscarriages, particularly among single women, as well as the concealment of normal childbearing, vitiate the results of any inquiry into the relative frequency of pregnancy. Conversely the exact percentage of women who have had gallstones rarely can be accurately determined. A survey of a large number of cases is necessary and each survey is subject to errors of interpretation or imperfect observation. Also, gallstones may have passed into the intestines through the bile ducts or through spontaneously developed fistulas, and their former presence thus escape detection.

deserves. Reference is made to the logical conclusion that gallstones in both men and women are formed almost exclusively during the active sex life of the individual. They are very rarely found in children and probably they appear only several years after puberty. Deaver and Ashhurst (44) said: "It is our belief based upon clinical experience, that most gallstones are formed between the ages of twenty and forty."

The proof that the production of gallstones ceases at or near the menopause is not so easy to verify. The widespread fallacy of confusing the symptoms of gallstones with the time of their formation especially in statistical summaries complicates the problem. It is unfortunate that much of the data about gallstone disease consists of references to "gallstone attacks," meaning either frank colic or more or less serious digestive disturbances. It is highly probable that the signs and symptoms of the presence of gallstones have absolutely nothing to do with the causes of their production. Therefore when it is argued that the menopause or a sedentary type of living or even obesity is conducive to the formation of gallstones the supporting facts which are cited often refer to clinical phenomena caused by the calculi, when as a matter of fact the gallstones themselves may have been present for many years without producing any recognizable signs. Carter and his co-workers (1939) clearly recognized this when they stated that their study [of 100 postoperative cases of gallstones] serves to emphasize the difficulty of determining the cause and pathogenesis of gallstones solely by study of the patient at the time of operation. The period of calculus formation may be limited and a study of the patient one to twenty five years later will fail to present the true picture of the condition determining the deposition of the stone." Whether gallstones are ever completely without signs or symptoms is largely an academic question. The fact remains that a relatively large number of individuals harbor gallstones which escape the notice of patients, relatives and attending physicians, and are discovered more or less accidentally at operation or at postmortem examination.

The comparatively narrow limits of time in which gallstones are usually produced in men and women were emphasized by Aschoff (11) when he wrote in 1931, "Cholesterol stones are formed during a relatively short period of life. Although it is possible that occasionally secondary formation of gallstones, particularly in badly diseased gall bladders may take place in the later decades of life there can be little doubt that the primary production of these calculi is confined to the third

fourth, and possibly fifth decades of life, that is, during the periods of sexual activity."

The third fact, closely related to the second, has likewise been largely neglected by most writers. In 1846 Hein noted that Sommering in his "*De Concrementis biliaria corporis humani*," published in 1795 asserted "Gallstones come 'auf einmal' [all at once] and not one after the other." In 1921 Knox expressed the same opinion when he wrote that gallstones are "usually in one crop" and the time of formation is relatively short. In the same year Roux and others stated, "The frequent presence in human gall bladders of large numbers of calculi of practically identical size and character has led to the general recognition of the importance in such instances of critical periods of stone inception and formation." Lichtman, in his book "*Diseases of the Liver Gallbladder and Bile Ducts*," published in 1942 also wrote about "fitters of gall stones" which might be formed in a short time as two months. In effect, this fact is based upon the well founded assumption that, whatever influences operate to produce gallstones, they are not constantly active in effective degree, and that gallstones are usually the result of a transient episode, which while it admittedly may be repeated, is not continuously in operation and is not of any marked frequency periodic or otherwise.

The fourth fact to which I wish to draw attention cannot be, and has never been, disputed by anyone but should be continually emphasized. This is that while the causes of gallstones, it is clear, act more effectively in women than in men, nevertheless, almost as many men as women have gallstones. In other words, whatever factors produce them in women the same factors operate with almost equal effectiveness in men. Here also the available evidence is wholly in favor of the view that in men as in women, gallstones originate during the period of sexual activity. Also, in this connection it may be particularly significant that several writers have presented data which imply that gallstones are produced in men, on the average at a later period of life (five to ten years) than in women. The data upon which this view is based are not conclusive, although highly suggestive. The conclusion depends largely on the fairly well established observation that gallstones are discovered at later ages among men than among

Exceptions to this generalization have been frequently noted. Gall stones have occasionally occurred in children (Kastner, 1911), and also, sporadically, gallstones have occurred in later years, after they are removed from the gall bladder by cholecystectomy. These exceptions do not, however, invalidate the fundamental theory of gallstone formation. Presumably variations or marked prolongation of the latent period is not known. Extensive study of such exceptions may lead to more valuable conclusions than the study of the routine or usual cases.

women. That is the peak of so-called incidence occurs almost one decade later in men. Dreyfus-Brissac (1883) noted that in women gallstones tended to occur between the ages of seventeen and forty two years, while in men the high point of incidence was between fifty and sixty. Scheel (1911) found at postmortem examinations that the same relative number of men and women had gallstones, only the men were twenty years older. Schmid (193) agreed with Dreyfus-Brissac and Scheel that gallstones occur earlier in women than in men—that is, between the twentieth and fortieth years. Aschoff (11) in one of his last papers (1931) referred to Lotm (1926) who demonstrated that the high point of the curve of gallstone incidence appeared earlier in women and reached its peak in the climacterium while in men this peak appeared between the ages of sixty and seventy years. Dublin and others (1934) reported from an analysis of insurance statistics, that gallbladder disturbances occurred in women at an earlier age than in men. For example 20.8 per cent of the affected women were under thirty years of age and 62.6 per cent were under forty years, while among the men with such disturbances the percentages for the corresponding ages were 13.1 and 47.3 respectively. Apropos of this theory is the fact that sexual maturity is usually reached at a later age in men than in women and also that it continues often many years, beyond the period of life when the menopause occurs in women.

The fifth fact, namely, that typical gallstones are formed almost exclusively in the gall bladder hardly needs any argument in its support. As Fowweather and Collinson (1927) expressed it, "Any inquiry into the cause of gallstone formation must be directed against the gallbladder itself." Surgeons and pathologists frequently find true biliary calculi in the common bile and hepatic bile ducts, and some of the surgeons are quite convinced that, at times, the calculi must originate in the bile ducts, because among other reasons when they are discovered they are too large to have passed through the apparently undilated cystic duct. Also occasionally when a considerable interval has elapsed after cholecystectomy and a thorough exploration of the bile ducts stones in the common bile duct have necessitated another operation or have been discovered at postmortem examination. Lahey in 1938 presented very convincing arguments in favor of this theory. How ever Phenister Aronsahn, and Peplinsky (1939) expressed the prevailing opinion when they stated, "Stones in a duct rarely if ever occur in the absence of cholelithiasis. My own personal experience confirms this opinion namely that

practically every gallstone found in the common bile duct or hepatic ducts could more rationally be ascribed to have originated in the gall bladder than in the bile ducts. The tendency of stones loose in the common bile duct to travel upward into the hepatic ducts or to be so completely imbedded in an apullalike dilatation of the distal portion of the common bile duct as to escape discovery is well recognized. The rare instances in which these two possibilities can be excluded should receive careful verification especially cases in which the gall bladder does not contain and in all likelihood never did contain calculi. The passage through the cystic duct of comparatively large stones without a residual permanent dilatation of that duct, and the possibility that tiny stones migrating from the gall bladder to the common bile duct later become enlarged by further deposits must be granted. Finally the character of the suspected primary stones in the common bile duct should be determined in order to be certain they correspond to the type of true gallstones and not to that of simple calcareous concretions which, at times, may be formed in any of the many different channels of the body.

Especially pertinent is the sixth fact namely that gallstones particularly those of the pure cholesterol type may be found in gall bladders, the walls of which are free from any demonstrable anatomic evidence of disease. Aschoff was the first to emphasize this point and many others have admitted or confirmed his conclusions. This fact is the best explanation for the occurrence of silent gallstones and any rational theory of the production of gallstones must be in harmony with this fundamental observation. Furthermore this fact is a direct refutation of the widely prevalent conception that bacterial infection is at the foundation of gallstone formation.

The argument that the infectious episode which caused gallstones might be transient and of such a benign character that there would be no residual anatomic traces was first expressed by Naunyn (151) in his original monograph *Klinik der Cholelithiasis* published in 1892 and was reiterated by him in subsequent papers. The theory became a real boon to certain clinicians and surgeons, notably Fraenkel (1918) Poppert (1921) Umber (1923) and others who found in it a convenient explanation for the occurrence of gallstones in normal gall bladders as well as an explanation for the presence of symptoms of gall-bladder disease such as colic, digestive disturbances, and jaundice in cases in which no stones were found at operation. These symptoms, together with the identification of bacteria especially the *escherichia coli*

in the normal bile were judged to be sufficient evidence in support of their conclusions and often justified for them, the removal of normal gall bladders. The advent of more logical explanations for both of these conditions, such as neurogenic dysfunction and the colloid theories of gallstone formation, has largely replaced the earlier notion of an infectious foundation for many diseases of the biliary tract. This theory aside from the fact that any theory which presupposes a bacterial infection profound enough to cause gallstones or to cause signs and symptoms of cholelithiasis when stones are not present and still produce no permanent alteration in the anatomic structures, is so contrary to all modern conceptions of infection and its results that only an insufficient knowledge of these conditions could excuse such faulty reasoning. This chapter in the development of knowledge of the pathogenesis of gallstones is an interesting example of the many devious trails which must be followed before well established truths come to light.

The importance of the exclusion of pathogenic micro-organisms from the list of primary factors in the etiology of cholelithiasis may not be fully realized. The subject has already been discussed (pages 7 and 8 of this article) but a few further comments seem to be justified. The huge volume of literature which deals with the presumed causal relation of bacteria to the production of gallstones is indeed imposing. It might be roughly divided into two phases. The first was the acquired urge to explain all pathological conditions by the premise of a primary infection with pathogenic bacteria. This tendency was and to some extent, still is a kind of obsession or "idée fixe." The second phase began with the admission that many diseases, including biliary lithiasis were primarily due to disorders which might conveniently be classified under the headings "metabolic" or "neurogenic." With such disorders, bacteria could only play a secondary or minor role. This distinction deserves emphasis. Clinicians, including surgeons, are naturally concerned with all the signs and symptoms of a diseased biliary system. Many of these manifestations, admittedly are due to infection of the bile passages by bacteria. Often such infections occur as complications to the presence of gallstones, especially after the calculi have interfered with the normal function of the gall bladder and bile ducts. Not only may infection of these structures by virulent micro-organisms occur in the absence of gallstones but also it has become increasingly evident in the last decade that functional derangements of the biliary tract can produce serious clinical phenomena, such as

pain colic, and even icterus, again without gallstones being held accountable. Even when the roentgen rays demonstrated gallstones, many keen clinicians were forced to realize that removal of the gall bladder (with the stones) did not always cure the fundamental condition.

Thus the frequent practice of writing about "cholecystic disease" as if there was only one entity with a common cause should be discouraged. As has been previously emphasized the production of gallstones in the anatomically normal gall bladder is largely a subclinical process and the consideration of their cause should be definitely separated from discussions of the causes and effects of the complications which may arise, often many years later from the presence of these stones.¹

Finally one more fact, the seventh, may or may not prove to be pertinent. I refer to the well known tendency for many gallstones to be spherical in shape. It is a common experience to find numerous small stones occasionally several thousands, all about the same size and composed of the same relative constituents and all remarkably round. Not only is the "epioid" character of this occurrence clearly manifest, but also some explanation is desirable to account for their almost perfect roundness. It is true that there is much evidence of the molding of gallstones both by the wall of the gall bladder and by contact with each other this latter influence being used to explain the frequent polyhedral shapes of the stones. But the spheres cannot be wholly accounted for by molding any more than can the many other round concretions in other parts of the body. Collections of such biliary calculi are never formed in a gall bladder closed by obstruction to the entrance of fresh bile and the supposition that colloidal phenomena of precipitation and aggregation are involved must receive serious consideration. Here also it is almost impossible to conceive how the presence of bacteria can play any role whatsoever.

SUMMARY

The principal data and theories embodied in the five important factors advanced in the past to explain the formation of gallstones have now been explored in some detail. Also seven more or less fundamental facts about gallstones and their occurrence have been presented. Some dead wood, such as stasis, infection irritative catarrhal cholangitis, and significant association with any other disease has been cleared away. Furthermore, as

Even more necessary is the effort to distinguish sharply the effects of gallstones and of other biliary disturbances from the mechanical obstruction of the biliary system, which occasionally lead to serious symptoms and discouraging attempts to effect relief.

reptance of the seven fairly well established facts about gallstones considerably narrows the field in which the ultimate etiologic determinants must operate. Any theory which adequately accounts for cholelithiasis must conform to these limitations and must also include and harmonize the remainder of the pertinent data which have been collected about this subject during the past several centuries.

Such a theory must explain why gallstones occur in both men and women, but more frequently and at an earlier age in the latter than in the former why they are formed almost exclusively during that period of life when sex functions are active why they are primarily almost without exception formed in the gall bladder and without any demonstrable anatomic changes in the wall of the gall bladder why they are produced during periods comparatively short in duration occasionally in showers or "litters" never continuously and which periods are rarely repeated and finally why gallstones tend to be rounded when not subject to molding influences by the wall of the gall bladder or by apposition to each other

With these conditions in mind, the conclusion becomes almost inescapable that gallstones occur only when there is a profound disturbance of biliary physiology induced by pathological deviations of hormonally controlled functions. Also in all probability the hormones which are concerned in this dysfunctional attack are those commonly designated as sex hormones, although any or all of the other hormones may be involved.¹

In order to produce gallstones this functional disturbance must result in, at least, two primary changes in the normal physiology of the gall bladder. One is an alteration in the composition of the bile. Theoretically this alteration might occur as a result of an abnormal secretory function of the liver cells. The characteristics of the bile are often profoundly affected by pathological changes in the hepatic parenchyma, but there is little evidence to connect these with cholelithiasis. As previously emphasized the changes in the constituents of the bile which lead to the formation of gallstones occur primarily in the gall bladder. So far as is now known, the most important of these changes is a relative diminution of the bile acids and their salts which are responsible for maintaining cholesterol bile pigment, and calcium in colloidal suspension. This decrease in bile salts is caused by their more or less selective absorption through the

gall-bladder walls into the capillary channels of the lymph stream and blood stream.

The second primary alteration is a radical change in the secretion of mucoid substances by the mucosa of the gall bladder. This change may be quantitative as well as qualitative, but probably qualitative alterations are more important. The physical differences which occur in mucin and related secretions of the mucosa of the gall bladder as well as of other mucosal surfaces of the body are well recognized but the chemical and pathological changes and their significance have not received the attention they deserve. In connection with the formation of gallstones, these mucoid substances, simultaneously with the reduction of bile acids must acquire some sort of coagulative property and form a binding substance and organic framework for the precipitated elements of the bile. Without this skeleton substance, bile sediments, which are frequently observed in the gall bladder bile ducts and bile obtained by duodenal drainage do not result in gallstones. The unincorporated precipitates are washed out of the bile passages and pass, usually harmlessly into the intestinal tract.

Combined changes, even to pathological degrees, in the absorptive and secretory functions of other structures that are lined with mucous membrane are not unknown or even unusual. Reactions of this type are most frequently observed in the mucosa and walls of the gastrointestinal tract, but nasal surfaces, bronchi, the walls of the prostatic acini and pancreatic ducts, and their mucous membranes under certain circumstances exhibit similar phenomena. In the gall bladder the colloidal dispersed elements normally concentrated and with discontinuous drainage may produce gallstones when the two alterations in the bile, which have been mentioned previously become effective, while in other parts of the body continuous drainage or lack of the cholesterol-bile-pigment-calcium complexes usually fails to cause calculi to form. The nearest approach to conditions comparable to those in the gall bladder occurs in the urinary tract and in the prostate gland where the corpora amylacea occasionally produce real concretions, and in the lungs, where similar structures form but very rarely become calcified.

The part that neurogenic factors play in the abnormalities of secretion and absorption has received increasing consideration. However neurological reactions sometimes are difficult to recognize or evaluate, particularly when exercised on internal organs. Also it must not be forgotten that the so-called dysfunctional states of the vegetative nervous system so well emphasized by

¹The expression "sex hormones" is misleading and inadequate. It is undoubtedly true that many purely sexual functions of the body are directly influenced by fairly specific hormones, but these are so closely interrelated with and, at times, with all the other hormones of the body that every vegetative, voluntary and psychic activity of the individual may be affected by them.

in the normal bile were judged to be sufficient evidence in support of their conclusions and often justified for them, the removal of normal gall bladders. The advent of more logical explanations for both of these conditions, such as neurogenic dysfunction and the colloid theories of gallstone formation, has largely replaced the earlier notion of an infectious foundation for many diseases of the biliary tract. This theory, aside from the fact that any theory which presupposes a bacterial infection profound enough to cause gallstones or to cause signs and symptoms of cholelithiasis when stones are not present and still produce no permanent alteration in the anatomic structures, is so contrary to all modern conceptions of infection and its results that only an insufficient knowledge of these conditions could excuse such faulty reasoning. This chapter in the development of knowledge of the pathogenesis of gallstones is an interesting example of the many devious trails which must be followed before well established truths come to light.

The importance of the exclusion of pathogenic micro-organisms from the list of primary factors in the etiology of cholelithiasis may not be fully realized. The subject has already been discussed (pages 7 and 8 of this article) but a few further comments seem to be justified. The huge volume of literature which deals with the presumed causal relation of bacteria to the production of gallstones is indeed imposing. It might be roughly divided into two phases. The first was the acquired urge to explain all pathological conditions by the premise of a primary infection with pathogenic bacteria. This tendency was and to some extent still is, a kind of obsession or "idée fixe." The second phase began with the admission that many diseases, including biliary lithiasis, were primarily due to disorders which might conveniently be classified under the headings "metabolic" or "neurogenic." With such disorders, bacteria could only play a secondary or minor role. This distinction deserves emphasis. Clinicians, including surgeons, are naturally concerned with all the signs and symptoms of a diseased biliary system. Many of these manifestations admittedly, are due to infection of the bile passages by bacteria. Often such infections occur as complications to the presence of gallstones, especially after the calculi have interfered with the normal function of the gall bladder and bile ducts. Not only may infection of these structures by virulent micro-organisms occur in the absence of gallstones but also it has become increasingly evident in the last decade that functional derangements of the biliary tract can produce serious clinical phenomena, such as

pain, colic, and even icterus, again without gallstones being held accountable. Even when the roentgen rays demonstrated gallstones, many keen clinicians were forced to realize that removal of the gall bladder (with the stones) did not always cure the fundamental condition.

Thus the frequent practice of writing about cholecystic disease as if there was only one entity with a common cause should be discouraged. As has been previously emphasized, the production of gallstones in the anatomically normal gall bladder is largely a subclinical process and the consideration of their cause should be definitely separated from discussions of the causes and effects of the complications which may arise often many years later from the presence of these stones.¹

Finally one more fact the seventh, may or may not prove to be pertinent. I refer to the well known tendency for many gallstones to be spherical in shape. It is a common experience to find numerous small stones occasionally several thousands all about the same size and composed of the same relative constituents and all remarkably round. Not only is the "episodic" character of this occurrence clearly manifest but also some explanation is desirable to account for their almost perfect roundness. It is true that there is much evidence of the molding of gallstones both by the wall of the gall bladder and by contact with each other this latter influence being used to explain the frequent polyhedral shapes of the stones. But the spheres cannot be wholly accounted for by molding any more than can the many other round concretions in other parts of the body. Collections of such biliary calculi are never formed in a gall bladder closed by obstruction to the entrance of fresh bile and the supposition that colloid phenomena of precipitation and aggregation are involved must receive serious consideration. Here, also it is almost impossible to conceive how the presence of bacteria can play any role whatever.

SUMMARY

The principal data and theories embodied in the five important factors advanced in the past to explain the formation of gallstones have now been explored in some detail. Also, seven more or less fundamental facts about gallstones and their occurrence have been presented. Some dead wood, such as stasis, infection irritative catarrhal cholangitis, and significant association with any other disease, has been cleared away. Furthermore it

Even more necessary is the effort to distinguish sharply the effects of gallstones and the resulting clinical disturbances from the noncalculous causes of the biliary system, which occasionally lead to similar symptoms and discouraging attempts to effect relief.

ceptance of the seven fairly well established facts about gallstones considerably narrows the field in which the ultimate etiologic determinants must operate. Any theory which adequately accounts for cholelithiasis must conform to these limitations and must also include and harmonize the remainder of the pertinent data which have been collected about this subject during the past several centuries.

Such a theory must explain why gallstones occur in both men and women, but more frequently and at an earlier age in the latter than in the former why they are formed almost exclusively during that period of life when sex functions are active why they are primarily almost without exception, formed in the gall bladder and without any demonstrable anatomic changes in the wall of the gall bladder why they are produced during periods comparatively short in duration occasionally in showers or "litters" never continuously and which periods are rarely repeated and finally why gallstones tend to be rounded when not subject to molding influences by the wall of the gall bladder or by apposition to each other.

With these conditions in mind the conclusion becomes almost inescapable that gallstones occur only when there is a profound disturbance of biliary physiology induced by pathological deviations of hormonally controlled functions. Also in all probability the hormones which are concerned in this dysfunctional attack are those commonly designated as sex hormones although any or all of the other hormones may be involved¹.

In order to produce gallstones this functional disturbance must result in at least two primary changes in the normal physiology of the gall bladder. One is an alteration in the composition of the bile. Theoretically this alteration might occur as a result of an abnormal secretory function of the liver cells. The characteristics of the bile are often profoundly affected by pathological changes in the hepatic parenchyma, but there is little evidence to connect these with cholelithiasis. As previously emphasized the changes in the constituents of the bile which lead to the formation of gallstones occur primarily in the gall bladder. So far as is now known, the most important of these changes is a relative diminution of the bile acids and their salts, which are responsible for maintaining cholesterol, bile pigment, and calcium in colloidal suspension. This decrease in bile salts is caused by their more or less selective absorption through the

gall-bladder walls into the capillary channels of the lymph stream and blood stream.

The second primary alteration is a radical change in the secretion of mucoid substances by the mucosa of the gall bladder. This change may be quantitative as well as qualitative but probably qualitative alterations are more important. The physical differences which occur in mucin and related secretions of the mucosa of the gall bladder as well as of other mucosal surfaces of the body are well recognized but the chemical and pathological changes and their significance have not received the attention they deserve. In connection with the formation of gallstones, these mucoid substances, simultaneously with the reduction of bile acids, must acquire some sort of coagulative property and form a binding substance and organic framework for the precipitated elements of the bile. Without this skeleton substance, bile sediments, which are frequently observed in the gall bladder bile ducts, and bile obtained by duodenal drainage, do not result in gallstones. The unincorporated precipitates are washed out of the bile passages and pass, usually harmlessly into the intestinal tract.

Combined changes even to pathological degrees, in the absorptive and secretory functions of other structures that are lined with mucous membrane are not unknown or even unusual. Reactions of this type are most frequently observed in the mucosa and walls of the gastrointestinal tract, but nasal surfaces bronchi, the walls of the prostatic acini and pancreatic ducts and their mucous membranes under certain circumstances exhibit similar phenomena. In the gall bladder the colloidal dispersed elements, normally concentrated and with discontinuous drainage, may produce gallstones when the two alterations in the bile which have been mentioned previously become effective while in other parts of the body continuous drainage or lack of the cholesterol bile-pigment-calcium complexes usually fails to cause calculi to form. The nearest approach to conditions comparable to those in the gall bladder occurs in the urinary tract and in the prostate gland where the corpora amyloacea occasionally produce real concretions and in the lungs, where similar structures form but very rarely become calcified.

The part that neurogenic factors play in the abnormalities of secretion and absorption has received increasing consideration. However neurological reactions sometimes are difficult to recognize or evaluate particularly when exercised on internal organs. Also it must not be forgotten that the so-called dysfunctional states of the vegetative nervous system so well emphasized by

¹The expression "sex hormones" is misleading and inadequate. It is undoubtedly true that many purely sexual functions of the body are undoubtedly influenced by fairly specific hormones, but these are so closely interrelated with most, and, at times, with all the other hormones of the body that every vegetative, voluntary and psychic activity of the individual may be affected by them.

Westphal and his followers, are often preceded by pronounced psychic and other disturbances of the central nervous system. Gundermann (1930) in a discussion of biliary disease suggested that excitement such as anger or emotional upsets, might act as a cause. He located disorders of this nature in the region of the third ventricle of the brain. These emotional crises in turn according to him react on the vegetative nervous system. Weiss and English, in their book *Psychosomatic Medicine* (1943) wrote "The role of the emotions in the possible development of gall tract disease, in the precipitation of attacks of colic is a matter with which general medicine has not sufficiently concerned itself."

Functional and organic changes, chiefly in the hypothalamic region of the brain, undoubtedly influence secretory activities of the epithelial cells probably largely through alterations in vasomotor control. The cause of so-called peptic ulcers more and more has been ascribed to pathological psychical disturbances in these brain centers.

The exact mechanism by which attacks of hormonally excited neurogenic dysfunction associated with emotional upsets causes the wall of the undamaged gall bladder to absorb bile acids selectively and at the same time to secrete a pathological mucoid substance has not been demonstrated. Disordered sex functions probably play a major role, and as these are more prominently displayed by women than by men they account for the preponderance of the formation of gallstones during the active sex life of women. More study is needed to discover the nature of these upsets. They must have a fairly common pattern, they must occur on very infrequent occasions, and they should be detectable and perhaps preventable.

CONCLUSIONS

1. It is a well established fact that women are more liable to have gallstones than are men.

2. Gallstones occur almost exclusively in both men and women during the time of life when sex functions are active.

3. Any explanation of why gallstones are formed must be in harmony with these two facts.

4. The production of gallstones takes place, as a rule, only in the gall bladder.

5. Neither abnormal stasis of bile nor bacterial infection nor other disease is responsible for cholelithiasis.

6. The clinical symptoms and signs produced by the presence of gallstones have no relation to the etiologic factors of their formation and often occur many years after the gallstones are produced. Most gallstones, at the time of their in-

ception and often for many years afterward, are relatively silent.

7. Cholesterol, the chief constituent of gallstones, together with bile pigments and calcium, is normally held in a state of colloidal dispersion by bile acids and their salts.

8. A relative excess of cholesterol or decrease of bile salts may lead to a precipitation of the colloidal suspended elements of the bile.

9. A binding substance, most likely an excess of changed mucin or other related nucleo-albumin serves to mold and preserve the precipitated substances in the form of calculi. There is little evidence that mucin or nucleo-albumin can act as a precipitating medium.

10. In order that gallstones may be formed there must be simultaneous disturbances in both the absorptive and secretory function of the mucosa of the gall bladder and its walls.

11. During the time of active sex life of both men and women, neurogenic hormonally controlled disturbances, both in the central and the vegetative nervous systems, are frequent and occasionally cause profound functional changes, particularly in the vascular system, smooth muscles, and secretions. These influences are more pronounced in women than in men, but in both they at times cause serious alterations in the absorptive and secretory functions of the gall bladder produce a changed mucin or mucoid substance in the bile, and disturb the normal balance or ratio of cholesterol and bile salts.

12. Gallstones are primarily the result of functional disturbances which are effective only on infrequent occasions and are active over comparatively short periods of time although repetitions of their effects, as well as complications due to obstructive phenomena or secondary infections may at times, occur.

13. Functional upsets, primarily but not always, responsible for gallstones, should be distinguished from secondary or subsequent pathological conditions which often cause clearly recognizable and occasionally serious clinical diseases.

14. More study is indicated in order that the psychic and other neurogenic disturbances which produce gallstones may be recognized while in action and thus afford a sound basis for prophylaxis and treatment.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Wolf, J. W.: Thrombosis of the Cavernous Sinus with Hemolytic Streptococcal Bacteremia; Treatment by the Intravenous Injection of Sulfadiazine and Penicillin with Recovery. *Arch. Otolaryng. Chlc.*, 1944, 40: 33.

Wolf states that a boy of ten years made a complete recovery from thrombosis of the cavernous sinus with multiple thrombi in the right lung and kidney and hemolytic streptococcus bacteremia. The source of infection was a furuncle on the bridge of the nose. The therapeutic agents were sulfadiazine and penicillin. A total of 500,000 Oxford units of penicillin and 64 gm. of sulfadiazine was administered in a period of nineteen days. No ill effects were noted during the course of treatment.

Apologies were offered because the author did not confine himself to one therapeutic agent. However in view of the severity of the conditions present and the failure of sulfadiazine therapy in a previous case in the same hospital under another physician's care the author believed that the risk was too great to depend on one drug. Furthermore although he believed that he might be grossly criticized he stated that sulfadiazine given in large doses to produce a blood level of 18 mgm. or more per 100 cc. had a definite curative effect on septicemia, especially that caused by staphylococci, which bacilli were undoubtedly present in the original focus.

The author also points out that not until the blood level was 18 mgm. + did the disease show signs of abating, and that when either drug was used exclusively no change in the course of the disease was noted. Thus it is apparent that thrombosis of the cavernous sinus, a disease looked upon in the past as inevitably fatal, may now be cured by the use of large doses of a sulfonamide drug in combination with penicillin; however the patient must be kept under close observation.

JAMES C. BRASWELL, M.D.

Nicholson W. M., and Anderson, W. B.: Penicillin in the Treatment of Cavernous-Sinus Thrombophlebitis; Recovery with Unilateral Ascending Optic Atrophy. *J. Am. Med. Assoc.* 1944 126: 2.

A thirty year-old male was admitted to the hospital in a stuporous condition four days after the appearance of a small furuncle in the right anterior nares. A blow on the bridge of the nose the day after the onset was followed by pain, frontal headache and a chill within twenty-four hours.

On admission there was high fever, hemolytic staphylococcus bacteremia, bilateral exophthalmos, chemosis of the conjunctiva, edema of the face and

a dusky red discoloration of the skin indicating venous obstruction. A blood concentration of 75 mgm. per cent of sulfadiazine was determined on admission and an additional 7 gm. in twelve hours produced no improvement.

Penicillin was given for fourteen days, treatment starting with one intravenous dose of 10,000 units followed by subcutaneous injections totalling from 30,000 to 50,000 units daily. A return of headache and fever after five days was followed by a further course of penicillin for eight days at the rate of 30,000 units daily and in thirty-eight days the patient was able to leave the hospital.

On the twenty-second day, when the right eye could first be opened, it was found that vision was reduced to light perception and has so remained.

There was increased perivascular sheathing with constrictions of the proximal portions of the retinal artery and papilledema resulting in optic atrophy. The optic atrophy was probably secondary to embarrassment of the arterial circulation with ischemia and later edema of the retina. I.e. it was an ascending degeneration. JOHN R. LINDSEY M.D.

EYE

Siegel, R.: Buccal Mucous Membrane Grafts in Treatment of Burns of the Eye. *Arch. Ophth. Chlc.* 1944, 3: 64.

The author stresses the importance of immediate transplantation of buccal mucous membrane in the treatment of conjunctival and corneconjunctival burns. There are three stages of burns of the eye: simple inflammation, profuse exudation and necrosis. Grafting with mucous membrane should be done in cases of direct burns of the cornea with destruction of the perilimbal circulation. In direct burns of the cornea with questionable perilimbal circulation and in burns of the eyeball in which the cornea is not involved but in which the perilimbal circulation is destroyed.

Prompt grafting stimulates vascularization (which in turn provides nourishment to the cornea) and prevents formation of scar tissue with resultant symblepharon. With the exception of cases in which the entire perilimbal circulation is totally and irreversibly destroyed, grafting of mucous membrane shortens the healing process and offers a better prognosis.

In 5 cases of this series buccal mucous membrane was grafted and in 3 cases no grafting was done. Siegel concludes that every grave conjunctival or corneconjunctival burn should be treated by means of a graft of buccal mucous membrane as soon as possible after the injury if the vascular supply to the cornea is destroyed, especially in cases exposed to

war gases in which there is vascular interference in the perilimbal circulation. Preserved heterogenous conjunctiva and cadaver conjunctiva require further clinical trial.

JOSUVA ZUCKERMAN, M.D.

Stallard, H. B.: Retinal Detachment; 78 Cases in the Middle East. *Brit. M. J.*, 1944, 2, 339.

The results obtained in a series of 78 cases of detachment of the retina in the Middle East are reported. In discussing the management of this condition the author states that accurate localization of the tear or tears in the retina is essential. The edges of the tear are made to adhere by electrocoagulation, i.e. by diathermy applied to the surface of the sclera and penetrating the sclera and choroid to reach, but not to enter the retina. Fluid beneath the detachment is drained by penetrating diathermy needle punctures and suction or by trephining of the sclera puncture of the choroid and the production of choroidoretinal adhesions around the tear.

Of the 78 cases of retinal detachment 76 were operated upon by one technique operation was contraindicated in one case, and spontaneous recovery occurred in another. The procedure in these cases was a combination of surface diathermy of from 90 to 100 ma. applied for a period of eight seconds around the edges of the tear or several tears and penetrating diathermy. One or two (very rarely more than two) punctures were made in the sclera with a diathermy needle, and a current of 40 ma. was applied for one second. The inter retinal fluid was aspirated by a glass tube and rubber suction bulb applied to the sclera over the site of the diathermy penetration.

In this series there were 13 cases of cystic degeneration, 21 of chorioidoretinal degeneration, 3 of myopia, 23 of civil trauma, and 18 cases of military trauma. In the 13 cases of cystic degeneration the retina was successfully replaced, the tear was sealed and the visual field restored. In the 21 cases of chorioidoretinal degeneration the retina was replaced and the visual field restored. In the 3 cases of myopia, the retina was successfully replaced in 2 cases, and in the third case operation was followed by a vitreous hemorrhage and a localized retinal detachment. In 20 of the 23 cases of detachment following civil trauma, the operation was successful. Operation was done in 16 of the 18 cases of detachment following military trauma, and in 10 of these the retina was completely replaced.

The prognosis depends upon the type of case. It is favorable in early cases with a small retinal tear which is easily accessible, particularly if operation is performed within a month of the onset of the detachment, and more favorable if the tear is in the lower half of the retina.

JOSUVA ZUCKERMAN, M.D.

EAR

Campbell, P. A.: The Progress of Aviation Otolaryngology in World War II. *Laryngoscope*, 1944, 54, 387.

The author discusses a number of recent changes in various aspects of aviation otology. Up to date

considerable research effort has been expended in improving our concepts and adding to our knowledge of aviation otology. Advances have been made in determining the effect of aircraft noise upon the ear and the effect of noise upon communications intelligibility. A number of tests are in the process of development. Protection against noise and research in airsickness also show promising developments. Campbell believes that much excellent work will probably go unreported in detail until the war is over.

NOAH D. FABRICANT, M.D.

Collins, E. G.: Injury to the Ear Among Battle Casualties of the Western Desert. *J. Lar. Otol. Lond.*, 1944, 59, 1.

In this investigation of 885 battle casualties of all types it was found that 1 in every 5 patients sustained some aural trauma, which was usually due to blast. The unit distribution of the patients and the types of battle casualties are shown in addition to the type of missile which caused the injuries.

In the majority of patients the aural injury consisted of a rupture of the tympanic membrane which was accompanied by an initial mixed inner and middle ear deafness in about 40 per cent of the patients with traumatic perforations. The percentage of patients with rupture of the tympanic membrane who are left with residual deafness is undetermined but is not considered to be negligible.

The effect of blast on the anatomical parts of the ear is discussed. Twenty two per cent of the traumatic perforations became infected.

Some observations are made on prophylaxis and the forms of treatment which proved of value.

JOHN F. DEXLER, M.D.

Birrell, J. F.: A Comparative Report on Ear, Nose and Throat Injury in the Army at Home and Overseas. *J. Lar. Otol.*, Lond., 1944, 59, 16.

The author has kept accurate notes on all of the cases which were examined and treated during his service as an Army ear, nose and throat specialist in a Military Hospital at home and in a General Hospital attached to the British North African Force. The article is replete with many tables and comparative figures on various phases of otolaryngology and certain conclusions and opinions are given.

There was a higher proportion of ear cases seen overseas than at home. These comprised a large percentage of otitis externa, but there was a marked similarity in the number of chronic cases of otitis media which were observed. Of the 4,000 unselected cases 57 per cent were aural. The most common conditions are chronic otitis media, otitis externa, chronic sinusitis and chronic tonsillitis in the order given.

JOHN F. DEXLER, M.D.

Brunner, H.: The Present Status of Diagnosis and Management of Ménière's Syndrome. *Arch. Otol. Chlc.*, 1944, 40, 38.

Brunner states that the typical Ménière attack consists of tinnitus, diminution of hearing, labyrinth

thine vertigo and spontaneous nystagmus. Only vertigo of the type which can be produced by the usual clinical methods of examining the labyrinth should be considered as labyrinthine.

Marked spontaneous nystagmus between Ménière attacks is not of labyrinthine origin. It indicates an organic disease in the posterior cranial fossa.

If the attacks consist only of labyrinthine or only of cochlear symptoms, a definite diagnosis cannot be made unless the patient is under longer observation.

During remission the patient is either normal, or, if the injury is progressive, he will present gradual diminution of function of the inner ear.

If there is a systemic, cerebral or aural cause the syndrome is called "symptomatic Ménière's syndrome." When no etiological factor can be determined the disease is designated "idiopathic Ménière's syndrome." The pathological changes are apparently the same in both cases.

Concerning the cause of Ménière's syndrome the metabolic theory and the vascular theory are offered. The metabolic theory is not supported by microscopic observation of the human ear as well as by experiment, and it explains the pathological picture of the idiopathic as well as the symptomatic Ménière's syndrome, although further studies are necessary.

Most frequently the angioneurotic disturbances within the internal ear are due to arteriosclerosis of the brain. Incipient arteriosclerosis of the brain should be taken into consideration in any case of Ménière's syndrome in which the first attack takes place between the third and the fifth decade of life and in which there is no evidence of another cause such as tabes, injury of the head or small tumor of the acoustic nerve.

Among the systemic diseases various types of leucemia, syphilis, influenza, malaria, virus infection, and particularly focal infection may cause the symptomatic Ménière's syndrome.

Allergy is occasionally but not frequently a cause of the symptomatic Ménière's syndrome.

Among the aural diseases a chronic adhesive process of the tympanic cavity is frequently found to cause the symptomatic Ménière's syndrome.

Concerning treatment, a Ménière neurosis must be excluded. When Ménière's syndrome is symptomatic, the etiological disease should be treated. There is no satisfactory treatment for the idiopathic Ménière's syndrome. Surgical intervention is indicated if the diagnosis of Ménière's syndrome is certain, if conservative measures have been exhausted, and if the disease is progressive on one side while the other ear is normal.

JAMES C. BRANWELL, M.D.

NOSE AND SINUSES

Ruskin, S. L.: Vitamin C-Sulfonamide Compounds in the Healing of Wounds; The Use of Sulfanilamide Ascorbate in the Treatment of Chronic Suppuration of the Wound After Radical Blunt Osteotomy. *Arch. Otolaryng.*, 1944, 4, 15.

The role of vitamin C in wound healing, declares Ruskin is now firmly established and its routine

use in all surgical and traumatic cases is indicated. It should also be used in conjunction with other therapeutic agents in cases of infection. Ascorbic acid stimulates the healing of wounds and counteracts the delay in healing incident to the use of sulfonamide compounds. Sulfanilamide ascorbate and sulfathiazole ascorbate both show a definite capacity to heal chronic suppurative otitic infections and to stimulate healing with epithelization.

NOAH D. FARRCAST, M.D.

Dandy, W. E.: The Treatment of Rhinorrhea and Otorrhea. *Arch. Surg.* 1944, 49, 75.

Rhinorrhea and otorrhea are due to the presence of a fistula connecting the cerebrospinal spaces with the exterior. Pneumocephalus may be associated with this condition. The two great causes of rhinorrhea and otorrhea are fractures of the skull and openings created by surgical procedures. Less frequent causes are erosion by tumors or infection, and congenital abnormalities. Post-traumatic otorrhea will usually stop in less than two weeks and there is consequently no indication for surgical intervention. Fistulas into the frontal or ethmoid sinuses or fistulas created by operation on the mastoid are frequently slow to heal or may close and reopen periodically.

A cerebrospinal fistula is always a potential source of meningitis or brain abscess. A fistula should never be left open longer than two weeks unless the fluid is unmistakably diminishing.

When rhinorrhea follows an operative procedure, the site of the fistula is along the path of the operative attack. It is, therefore, not usually difficult to find. If the fistula follows a depressed skull fracture, the depression may indicate its position. If there is no depression, roentgenograms including the frontal, ethmoid, and sphenoid sinuses are extremely important. In frontal craniotomy an unusually large frontal sinus may be opened. It is of the greatest importance that the surgeon should always know the size of the frontal sinus as demonstrated in roentgenograms before he uses a low frontal approach. When a frontal sinus is opened a flap of dura can be reflected over the opening and tightly sutured to the overlying galea. If the opening is disclosed by rhinorrhea after the operation is completed, the wound should be reopened immediately and the procedure carried out. During cerebellar operation a mastoid cell is occasionally opened in this event the dura should be immediately sutured over it to prevent immediate or subsequent infection.

In 3 of 4 cases in this series in which otorrhea followed operation on the mastoid, the bony defect was in the roof of the petrous bone about 3 cm. beside of the lateral wall of the skull. Therefore, this is the logical place to look for the fistula. The corresponding dural defect can be sutured and, if necessary, re-enforced by a piece of fascia lata or more conveniently by a layer of the sheath of the temporal muscle. If the dural defect is near the surface the fascia is sutured in place. If the fascia is too

stick it can be laid over the suture line and treated with a 3.5 per cent solution of iodine to promote adhesions.

The author has encountered 11 cases in nearly twenty years and these are reported in some detail.

HAROLD C. OCHSNER, M.D.

MOUTH

Somervell T. H.: Recent Advances in the Treatment of Carcinoma of the Mouth and Jaws. *Brit J Surg* 1944 32 35

Epithelioma of the mouth is so common as to be considered indigenous in the coastal districts of South India and Ceylon. In a 200-bed hospital at Travancore 500 operations have been done yearly for malignant diseases of which nearly 75 per cent occurred in the mouth. The site was the cheek lips, or lower jaw in 80 per cent, the tongue in 13 per cent and the upper jaw in 7 per cent. This high incidence of cancer of the mouth is attributed to the use of tobacco along with the betel leaf and areca nut. The combination of lime made from shells with two particular brands of tobacco used in that area is considered to be the most important etiological factor.

The treatment most suited to the various regions is discussed. Cancer of the cheek and lip is removed

by diathermy with implantation of radium needles at the time of operation followed later by resection of the glands and the further implantation of radium. Extraction of the teeth and removal of the glands is done after removal of the growth. For cancer of the jaws surgical removal is preferred with removal of the glands and the insertion of radium needles. Chloroform has been found the most suitable anesthetic.

Cancer of the tongue if involving only the tip may be removed by diathermy otherwise it is treated by the insertion of radium needles and later resection of the glands.

Cancer of the tonsil the epiglottis and the nasopharynx is treated with radium needles. Removal of one side of the hard palate may be necessary to permit access to the nasopharynx.

Glands of the neck are removed surgically and radium needles implanted at operation when complete removal is questionable.

The necessity of radical surgery is emphasized along with the liberal use of radium needles, which must be available for insertion at the time of operation.

Deep x ray therapy has been generally unsatisfactory in the author's experience.

JOHN R. LINDHAY, M.D.

SURGERY OF THE NERVOUS SYSTEM

PERIPHERAL NERVES

Russell, W. R. and Harrington A. B.: Early Diagnosis of Peripheral Nerve Injuries in Battle Casualties *Br J M J* 1944 2 4

Delay in the early diagnosis of peripheral nerve injuries following war wounds has gravely prejudiced the subsequent usefulness of limbs in many cases according to the study made by the authors. They stress the importance of an early examination for peripheral-nerve injuries and outline the salient points in diagnosing peripheral nerve lesions of the upper and lower extremities. Motor and sensory tests can be carried out, in a high percentage of patients in a very few minutes and a record made of the nerves involved and the relative extent of their injuries.

The authors have described, in a clear concise fashion the important points in examination with reference to each of the major nerve trunks. They have also described certain unusual movements that can be accomplished by patients with complete paralysis of one nerve by substituting other muscles or because of an adjacent nerve overlap.

Suggestions are made as to a method of recording nerve function by chart, by lifting the major nerve trunks and giving estimates of the function in the muscles supplied by that particular nerve and by grading these estimates from 0 to 5 according to the amount of muscle contraction present.

One of the most important points in this article emphasizes the harm that may ensue to muscles and joints by extensive and improper splinting. It is advised that in forward surgery near the front, no effort or attempt be made to support paralyzed muscles except by using a sling and advising the patient to prevent overstretching of the paralyzed muscles as far as possible.

Extensive casts or splints have resulted in so-called frozen hands, which quickly lead to a damaging vicious cycle, as follows: the hand is kept immobile, the joints become stiff, the hand becomes painful, the patient is even more unwilling to move his hand, et cetera. The early active movement of joints should be encouraged. Passive exercise by the patient can often be carried out even when physical therapy is not available.

HOWARD A. BROWN, M.D.

Denny Brown, D., and Brenner C.: Lesion in Peripheral Nerve Resulting from Compression by Spring Clip *Arch. Year Psychiat., Chic.*, 944 53:1

Experiments have been conducted to determine the effect of a compression lesion of a peripheral nerve both insofar as the local changes in the nerve are concerned and with reference to its peripheral function as well.

A special spring clip was devised the tension of which could be measured in grams, and the experiments were performed on cats under pentobarbital-sodium anesthesia. The operative studies included different degrees of pressure and a varying time element with regard to the compression of the nerve. Subsequently the nerve was again exposed under anesthesia and stimulated electrically above and below the spring clip before the animal was sacrificed. Following this the nerves were fixed, stained with osmic acid and sectioned in paraffine or they were embedded in pyroxylin and stained by the Grobelschowsky the Nissl, or the iron hematoxylin method. As a control the sciatic nerve on the opposite leg was clamped with a hemostat for ten seconds, which produced a complete lesion. This allowed of comparison from the standpoint of function peripheral to the point of the lesion.

Metal clips exerting a tension of 170 up to 430 gm. left in place for two hours, produced a transient paralysis lasting from five to eighteen days. There was no demonstrable gross defect in sensation and the distal portion of the nerve fibers did not degenerate. Microscopic study revealed an intermittent loss of myelin at the nodes of Ranvier in the area compressed. This lesion is said to be identical with that produced by compression of the nerve with a tourniquet. Motor recovery was fairly early, but the restitution of the myelin defect was only slight at an interval of from six to eight weeks following the trauma and defects were still demonstrable after six months.

Clips having a very much lower degree of tension (2.5, and 7 gm.) were then used and these could be left in place as long as fourteen days without their producing any defect in conduction—whether tested by walking ability, placing reactions, spreading of the toes or reaction to pinch of the toe pads in the unanesthetized animal, or by stimulation of the exposed nerve above and below the clip with the animal under light anesthesia. Despite the lack of these changes, the compressed segment of nerve showed marked narrowing, and was edematous on either side of the region of constriction. There were rather marked histological changes present in the myelin and axis-cylinder in the edematous region. This appeared to be due to simple swelling of the myelin, and was associated with the mobilization of large pale endoneurial cells.

A 44-gm. clip, when left in place, produced a complete motor and sensory paralysis, and exploration after fifteen days revealed complete loss of all electrical excitability in both the sensory and motor fibers below the clip, and complete histological degeneration of all the fibers in the nerve and of all the motor and nerve endings with atrophy of the muscle fibers. The proximal degeneration was of the type due to excessive ischemia.

Continuous compression by clips of from 9 to 10 gm. produced delayed paralysis, which appeared on the fifth to the eighth day and lasted up to twenty five days with recovery without necessarily any wallerian degeneration or change in the nerve endings or muscles. There was however segmental loss of myelin and there were changes due to edema.

The effect of pressure on nerve is considered to be due entirely to ischemia and the characteristic histological lesion and dissociated paralysis form a distinctive type of neuropathological reaction. The histological evidence indicates that the dissociation between sensory and motor function is due to a functional property of the disorder of the axoplasm, and not to selective effects related to the size of the fibers.

HOWARD A. BROWN M.D.

Jelasma, F : Clinical Analysis of 1 000 Consecutive Cases of Low Back Pain with Particular Reference to Sciatic Pain Caused by Extrusion of the Intervertebral Disc. *South. M. J.*, 1944 37 372.

Clinical analysis of 1,000 consecutive cases of low back pain revealed the fact that 531 presented sufficient clinical signs and symptoms to warrant the assumption that a focal neurological lesion was present. The remainder or 469 did not present any focal neurological signs.

Of the 531 focal lesions approximately 9 per cent were due to conditions other than herniated disc. These conditions consisted of traumatic injury to the bodies of the vertebrae metastatic tumors of the spine spinal-cord tumors, and spina bifida occulta.

It was found that palliative measures and conservative treatment are definitely indicated and give good results.

In a very high percentage of cases the onset of the trouble can definitely be ascribed to injury.

The incidence is highest between the ages of thirty and forty, a time when men are still active yet the disc is definitely less able to withstand trauma.

Multiple intervertebral discs were found in 7 per cent of the cases.

The clinical syndrome of extruded discs in the lower lumbar region is well known to make the use of myelograms unnecessary except in a very few cases.

The results are favorable in the cases with definite root pain if the root is carefully explored and the lesion completely removed.

JOHN J. MALONEY M.D.

BRAIN AND ITS COVERINGS CRANIAL NERVES

Adrian, E. D : Localization in the Cerebrum and Cerebellum. *Brit. M. J.*, 1944 2 137

Attention is called to the newer methods of physiological technique with regard to the study of localization in the cerebrum and cerebellum. Animal studies made under anesthetics of the barbitalur group, are described first, with reference to stimulation of various portions of the retina, and the correlation

between this and electrical activity demonstrated in the striate area of the brain at the same time. Stimulation of various portions of the retina can be shown to affect different portions of the striate area from an electrical standpoint. A diagrammatic scheme is shown which indicates the localization of stimulation of various parts of the retina and its representation in the visual area of the monkey's brain.

The author describes his study of the nervous mechanism of the cochlea in cats and also in monkeys. He found that when the cochlea is stimulated by sound electrical activity appears in the appropriate region the upper surface of the superior temporal gyrus. With notes of low pitch the maximum activity in monkeys is in the anterolateral part of the receiving area, and with high notes in the posteromedian part of the receiving area. Thus it would appear that the apex of the cochlea supplies the anterolateral part and the basal turn the posteromedian part.

The relation of the brain to the sense organs is illustrated by the difference in the receiving areas of the brain in the cat and in the pig, with special reference to the forelimb area. In the cat one finds a very large forelimb area of representation in the cortex with individual areas representing the digit footpad etc. whereas in the pig the area chiefly represented is the snout, and it is difficult or impossible to detect anything at all from the limbs. This, presumably, is because the cat uses its forelimbs and claws in skilled movements which must be guided by sight and touch, whereas the pig uses its limbs for standing and walking, and for nothing else. All skilled movements of the pig are made by the snout, and this has an elaborate representation in the brain.

The author's study includes a brief discussion with regard to the role of the cerebellum. Here, localization has not been particularly satisfactory experimental work on animals would seem to indicate that impulses from the hindlimbs are registered more anteriorly in the cerebellum, while those of the face and head area appear to lie more posteriorly. A good deal of the cerebellum seems to lack any local representation of the body and limbs.

HOWARD A. BROWN M.D.

Babeon, B. G : Spontaneous Subarachnoid Hemorrhage in Infants and Its Relation to Hydrocephalus. *J. Pediat.* S. Louis, 1944, 25 63.

Blood in the spinal fluid of the newborn infant usually occurs as the result of birth trauma or hemorrhagic disease. These conditions are well established during the first week of life. Three cases are reported in which spontaneous hemorrhage occurred in infants between the ages of eighteen and thirty days. Two of the patients were siblings. The bleeding apparently developed suddenly without evidence of hemorrhage at any other point. Evidence of acute infection scurvy purpura hemophilia, or leucemia was lacking in all cases, and the late onset made hemorrhagic disease of the newborn infant seem unlikely. Subsidence of bleeding occurred

promptly in all cases and no cause for the bleeding could be determined. Two of the patients developed hydrocephalus. Of these one succumbed from pneumonia after operation was attempted to cauterize the choroid plexus; the other, now five years of age, has an arrested hydrocephalus of considerable size.

Spontaneous subarachnoid hemorrhage occurs in children about as frequently as in adults and although death and residual paralysis are common, approximately 50 per cent recover completely. The cause is generally rupture of a congenital defect in a cerebral vessel. This is presumed to be the cause in the cases reported since disease and dyscrasia were ruled out. The reaction of the blood on the meninges with resultant adhesion and obstruction to the free flow of cerebrospinal fluid is presumably the cause of the hydrocephalus. It is suggested that unrecognized subarachnoid hemorrhage at birth is a likely cause of varying degrees of hydrocephalus and that prompt and complete removal of blood may offer the best chance of avoiding acquired hydrocephalus from such hemorrhage. JAMES L. LINDQUIST, M.D.

Newhill, H. P., and Anderson, G. C.: Racial and Sexual Incidence of Primary Intracranial Tumors: Statistical Study of 123 Cases Verified by Autopsy. *Arch. Nerv. Psychiat.* Chlc. 1944, 51: 364.

This is a statistical study based on the records of 6,112 consecutive autopsies of patients between the ages of one month and seventy years. It was conducted in a hospital which has a large number of negro patients. More than half of the autopsies were carried out on negroes. In the series 131 primary intracranial tumors were observed. Forty-five occurred in members of the negro race and 88 in members of the white race. Thus 1 of 47 white patients on whom autopsy was performed had a primary intracranial tumor while only 1 of 132 negro patients had such a tumor. This is more significant when one knows that 1,752 more autopsies were carried out on negroes than on white persons.

Very carefully prepared statistical tables are available and certain interesting conclusions were reached. Gliomas occurred twice as frequently in the white race as in the negro. This tumor was most frequently found in white females. Meningioma was three times as frequent in white persons as in negroes. Of the 28 meningiomas which were found, 12 occurred in white females. Other intracranial tumors showed no sexual or racial predilections.

ADAM V. VAN DUSEN, M.D.

SPINAL CORD AND ITS COVERINGS

Badal, D., Munro, D., and Lamb, M. E.: The Clinical Significance of Bacteriuria in Patients with Spinal-Cord Injuries. *N. England J. M.* 1944, 830: 683.

The most common organisms found in the urine of patients with spinal-cord injuries are the proteus vulgaris, Escherichia coli, alpha hemolytic strepto-

coccus, enterococcus, and staphylococcus. The presence of bacteria in the urine does not necessarily imply infection. Infection is manifested by chills and fever and the presence of 100 or more white cells per high power field in the urine.

Bacteriuria will develop in all cases with an indwelling catheter by the end of the first seventy-two hours. Sterilization of the urine in the presence of an indwelling catheter used as part of the tidal drainage apparatus has been impossible except by withdrawal of the catheter and is unnecessary provided that the latest type of apparatus is used and is properly adjusted to the bladder it is serving. Infection of the urinary tract as evidenced by the symptoms and signs of cystitis, pyelitis, and urethritis in a patient with a spinal-cord injury who is being treated with tidal drainage is best controlled by proper adjustment of the apparatus, bed rest, and the administration of large amounts (5,000 cc.) of fluid daily.

Patients who have had a spinal-cord injury and recover can expect to have a normal genitourinary tract with normal function and without bacteriuria, unless they have had a transection of the cord, a renal or bladder stone, a draining perineural abscess, or a lesion that has produced permanent physiological or anatomic denervation of the bladder. If such a patient has a transected spinal cord he can expect a reflex bladder without bacteriuria. If such a patient has had a physiological or anatomic denervation of the bladder he can expect a shrunken, useless bladder with bacteriuria and recurrent bouts of pyelitis. DAVID JOHN LEVINSKY, M.D.

French, J. D., and Payne, J. T.: Cauda-Equina Compression Syndrome with Herniated Nucleus Pulposus: A Report of 8 Cases. *Ann. Surg.* 1944, 70: 73.

Herniation of the nucleus pulposus in its more common form has been well described in the literature, but little can be found concerning extensive protrusions. The authors describe 8 cases of massive nucleus-pulposus protrusions in which the lesions produced either a complete or partial subarachnoid block with cauda-equina compression. The history of these patients so closely resembles that of patients with cauda-equina tumors that a differential diagnosis is difficult. In the authors' experience cauda-equina compression occurs more often from herniated nucleus pulposus than from tumor.

The duration of the symptoms varied from three weeks to thirty years. Most of the patients suffered a short, rapidly progressing period of incapacity just before their entry into the hospital. In none of the patients was there a history of a severe injury. The pathological process was found at L₁, L₄, and L₅. In all cases it severely compressed the dorsal sac. In 3 cases there was thickening of the arachnoid with matting of the cauda equina. In 2 of these cases this was present to the extent that obstruction remained after removal of the extruded nucleus pulposus.

There is considerable similarity in the symptoms. The main complaints were pain in the back and both legs, numbness in the saddle area and/or both legs, weakness and sphincter disturbances. The signs were also similar. These consisted of weakness or atrophy in the gluteal region or legs, sensory changes in both legs, multiple changes in the knee and ankle jerks and sphincter abnormalities. A narrowed interspace at the level of the protrusion was often found. This is an important diagnostic point in differentiating nucleus pulposus from tumor. The total protein of the spinal fluid varied from 60 to 630 mgm. per cent. DAVID JOHN IMPASTATO M.D.

MISCELLANEOUS

Friedman A. P., and Brenner C.: Post Traumatic and Histamine Headache *Arch. Neur. Psychiat.* Chic., 1944, 53: 126

This study represents an investigation of the relationship between the mechanism of post traumatic and histamine headache. Twenty two patients with a history of post traumatic headache were given 0.1 mgm. of histamine base (0.175 mgm. of histamine diphosphate) intravenously. The prompt decrease in systolic blood pressure occurring after the injection

of histamine was followed by a secondary rise in pressure of corresponding degree. Headache developed as the blood pressure was rising. The rise in pressure appears to be due to a reflex response of the sympathetic nervous system secondary to the immediate changes produced by histamine.

The headaches produced by this injection were identical in character and location with the post traumatic headaches experienced by 13 patients and were strikingly similar to those experienced by 3 patients. The results were particularly significant in those patients with asymmetric or unilateral post traumatic headaches accurately reproduced by histamine injection. It is reasonable to conclude that histamine activated the physiological mechanism involved in the production of post traumatic headache.

The majority of patients with histamine headache obtained some relief by sitting upright. This is inconsistent with reports that lowering of the intracranial pressure of the cerebrospinal fluid aggravates histamine headache.

A few patients who could be followed up reported a decided diminution in the frequency and severity of their headaches after they received the injection.

JOHN L. LAMOUR M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

D. Abreu, A. L., Litchfield, J. W., and Hodson, C. J.: Major Complications of Penetrating Wounds of the Chest. *Lancet* Lond., 1944, 247 197

The authors discuss several hundred penetrating wounds of the chest which occurred in Italy where infection seems to have been more prevalent than in North Africa. Most of the wounds were received from two to forty days prior to admittance of these cases at the General Hospital where the authors worked. There were 125 patients with uninfected hemothorax 77 with pyothorax, 34 with abdominal-thoracic wounds, 44 with proved atelectasis 16 with lung abscesses 23 with bronchopleural fistulas, 11 with extrapleural hemothorax and 84 with retained intrathoracic missiles (pulmonary in 55 pleural in 15 and mediastinal in 14).

There were 15 deaths 11 occurred one month after the injury. Gross empyema was the cause of death in 13 cases 1 patient died as a result of a heart wound and 1 from a severed thoracic duct.

Patients with uninfected hemothorax were treated by thorough aspiration and breathing exercises and all but the smallest effusions were aspirated. Air replacement was not given except to relieve respiratory distress or to aid in roentgenological diagnosis. Of 131 cases of hemothorax without any evidence of infection, 125 were rendered fluid-free and 5 became infected. Clotting in a hemothorax is often due to infection.

Seventy-seven cases of pyothorax with 13 deaths should correct any undue optimism with regard to penetrating wounds of the chest. The ideal treatment is to aspirate fluid until the lung has re-expanded enough to permit localization of the pus to a pocket. In the very grave cases surgery could not be delayed long enough to permit re-expansion of the lung and localization of the pus. The advent of penicillin has aided in checking the severe toxemia, and in delaying or avoiding, operation in some of these cases. Hour-glass saddle-shaped and multi-locular empyema cavities required the breaking down of some adhesions at operation. The procedure in such cases is described.

After operation, full drainage must be maintained. A constant watch by roentgenography must be kept on the size of the cavity and the open tube is kept in place until a pleurogram proves that no empyema cavity remains.

Penicillin therapy is of great value, its chief use is in the form of intrapleural instillation of the sodium salt combined with aspiration of infected pleural fluid and many heavily infected effusions have been sterilized. The authors describe the method of its use in the closure of infected wounds of the chest wall.

The late complications of 34 thoracoabdominal wounds included empyema, hemothorax, pleuro-biliary fistulas diaphragmatic tears subpleural abscess and pneumoperitoneum.

EARL O. LATIMER, M.D.

Parsons, W. H., Henthorne, J. C., and Clark, E. L., Jr.: Plasma-Cell Mastitis: Report of 5 Additional Cases. *Arch. Surg.* 1944, 49 86.

Since Adair described plasma-cell mastitis as a clinical entity in 1935 there have been approximately 45 cases reported. This lesion is characterized by a unilateral painless tumor which occurs in parous women. Sometimes mild and evanescent signs of inflammation are present in the course of its development, and occasionally there is a watery or creamy discharge from the nipple. Its most distinctive clinical feature is its striking resemblance to mammary carcinoma. It is not unusually tender. Often it is so adherent to the skin as to produce orange peel dimpling. The nipple is frequently retracted and the axillary lymph nodes are likely to be enlarged.

The gross lesion of plasma-cell mastitis appears as a yellowish brown discoloration of the mammary tissue often associated with the formation of abscesses. The contents of the abscess and of the contiguous ducts are puriform or butterlike.

Histologically there is an ulceration of the duct epithelium, which is replaced by granulation tissue, the formation of foreign-body giant cells, and a periductal collection of plasma cells and other leukocytes. Sheaves of fatty acid crystals and other evidences of the presence of lipid substances, such as foamy histiocytes and droplets of fat within the plasma cells, have been described.

The authors observed 5 cases of plasma-cell mastitis in 1500 specimens of breast tissue examined. There was a recurrence of the lesion in 3 patients. There was diffuse comedonastitis coexisting in 1 case. One patient went through a normal pregnancy in the same year that her breast was removed without the development of mastitis in the remaining breast. In 1 patient who had both ovaries removed five years prior to the onset of symptoms referable to the breast, the course of the plasma-cell mastitis covered three years which is an unusually prolonged time for this condition. EARL O. LATIMER, M.D.

TRACHEA, LUNGS, AND PLEURA

Goorwitch, J.: Closed Intrapleural Pneumothorax. *J. Thorac. Surg.* 1944, 3 5.

This study deals with the author's personal experience with internal pneumonolysis as well as an analysis of over 7,000 cases reported in the literature since 1924. The series includes 55 operations performed by the author on 50 lungs of 48 patients, as

well as 2043 cases collected from the literature by Moore from 1924 to 1932 and 5114 cases collected by the author from the literature from 1933 to 1944.

As a rule more adhesions were found thoroscopically than would be expected from a study of the roentgenograms. Complications occurring in the author's cases included fever in 44 per cent, serous effusion in 11 per cent, spontaneous pneumothorax in 3.6 per cent, extension of the disease in 3.6 per cent and hemorrhage, severe emphysema, and obliterative pleuritis each in 1.8 per cent.

In the collected cases fever was found to occur in about one fourth of the cases, hemorrhage was infrequent but accounted for 9 deaths among more than 7,000 cases, spontaneous pneumothorax is regarded as a serious complication and accounted for 9 per cent of all deaths in the collected series, pleural effusions occurred in about 25 per cent of the collected cases, bronchopleural fistulas and empyema occurred infrequently but they are the largest single cause of death.

In general the clinical results were reported as satisfactory in 75 per cent of the cases. The author believes, however, that this terminology should be discarded, as the clinical result depends on the effectiveness of the pneumothorax. Closed pneumonolysis is evaluated with respect to complications and clinical results. THOMAS F. THORNTON, JR., M.D.

Bayliss, C. G.: Closed Intrapleural Pneumonolysis.
Med J Australia 1944 2 129

Systematic, despite the great breadth of the subject treated, this disquisition begins with the history of artificial pneumothorax, to be followed by that of pneumonolysis and reviews the more recent literature on the structure of adhesions in pulmonary tuberculosis, the technique of operation (the author has employed exclusively the galvanocautery) anesthesia (nembutal, 3 gr. two hours before operation, and omnopon 0.5 per cent, with adrenalin 1 in 1000) and puncture sites. The author nearly always chooses the anterior axillary line for either the thoracoscope or the cautery, occasionally he chooses the posterior axillary line for the thoracoscope, the height of the puncture depending upon the location of the adhesions to be severed. The adhesions are "freed" released or enucleated rather than cut, the line of separation being external to the parietal pleura.

The basis of the report consists of 143 operations on 115 patients. In 65 of these individuals (56.5 per cent) complete pneumonolysis was accomplished, the presence of tubercles on the pleural surfaces not preventing the operation so long as they were not too close to the adhesion to be severed. In 35 per cent the operation remained incomplete and in 15 (13 per cent) a thoroscopic inspection was all that was attempted. The youngest patient operated upon was fifteen years of age. In 57 cases of this material, the disease was active in the contralateral lung at the time of operation, in 2 cases there was present roentgenographically a "doubtful" area. In

7 instances contralateral artificial pneumothorax was being maintained at the time of operation. The operation was always instituted as soon as possible, there was no waiting for the full attainable effects of the pneumothorax (in 35 patients artificial pneumothorax had been present for less than three months, in 34 from six to twelve months, in 6 from twelve to eighteen months, in 4, over eighteen months). The author has never countenanced artificial pneumothorax under positive pressure in an attempt to obtain better conditions for pneumonolysis.

It is considered that the operation was successful in 58 instances, unsuccessful in 48 (including 15 patients in whom pneumonolysis was not attempted). In 12 individuals the time has been too short to permit of final assessment of the results. Complications were hemorrhage (3 patients, in 1 the source was the thoracoscopic puncture wound), persistent nonpurulent effusion (88 per cent of the operative patients exhibited some serious effusion but in only 4 was it extensive or persistent enough to require special notice), probably tuberculous in origin, spontaneous pneumothorax, empyema (7 patients of whom detailed case histories are given) and contralateral spread of the disease. Less important complications seen include surgical emphysema, postoperative vomiting, injury to nerves, air embolism, pleurocutaneous fistula and dyspnea during operation.

None of these complications seemed to be due to the operation per se, particularly there seemed to be no harmful effects from the "smoke" of the galvanocautery, none of the complications seemed to emporate the original tuberculous condition, and there was only 1 death (due to valvular spontaneous pneumothorax) which was ascribable to the secondary effects of the operation of pneumonolysis.

JOHN W. BRENNAN, M.D.

Edwards, P. W., Penman, A. G., and Logan, J.: Late Results of Closed Intrapleural Pneumonolysis.
Brit M J., 1944, 2 270

In 1939 Edwards reported the immediate results of intrapleural pneumolysis on 235 patients. These patients have now been followed up for a period of five years. Bilateral operations and thorascopies without division of adhesions have been excluded from this series, which brought the number down to 200 consecutive cases of pulmonary tuberculosis treated by artificial pneumothorax, with unilateral division of the adhesions by closed intrapleural pneumolysis. When the indications existed (in 110 cases) this treatment was supplemented by phrenic avulsion. All of the patients underwent a strict course of sanatorium routine.

Of the 200 patients, 2 were lost sight of in this period, 133 (66.5 per cent) survived five years, 71 (86.5 per cent) in whom a satisfactory collapse was obtained by operation survived five years, and 56 of these were well and working after six years, none had a satisfactory collapse before operation.

A satisfactory collapse on one side seemed to greatly improve the prospect of survival in cases with bilateral cavitation.

Sputum was negative or absent three months after operation in 138 (70 per cent) of the 193 patients who were followed up. Of these sputum-negative patients, 100 (70 per cent) survived five years compared with only a 40 per cent survival in the sputum positive group. The great majority of the negative findings were confirmed by concentration and culture. The persistence of positive sputum three months after division of the adhesions indicates a poor prognosis. On the other hand a negative sputum improves the outlook in the incomplete and "ineffective" collapse groups.

Tuberculous empyema especially when secondary infection is present is a serious complication, but it accounted for only 18 per cent of the deaths in five years.

If artificial pneumothorax is employed the aim should be to obtain the most complete collapse possible by the use of intrapleural pneumolysis.

The authors have found that the collapse obtained as the result of an extensive cauterization was no less effective than that in which smaller or fewer adhesions were divided.

In those patients on whom operation carries special risk by reason of the anatomical character of the adhesions or because of the poor general condition of the subject, alternatives to artificial pneumothorax must be considered. However when contralateral disease allows of no more radical alternative the operative risk must be accepted for success in obtaining a satisfactory collapse carries with it some prospect of improvement in the contralateral disease. The abandonment of the pneumothorax without thoracoscopy and the maintenance of an unsatisfactory collapse are both bad practice.

JOSEPH K. NARAT, M.D.

Butler, E. G. B., Perry, K. M. A., and Valentine, F. C. O.: Penicillin in Acute Empyema. *Brit. M. J.*, 1944, 172.

The authors report the results of their experience in the treatment of 18 cases of acute empyema by means of aspiration and the injection of penicillin into the empyema cavity. The amount of penicillin used varied from 10,000 to 40,000 units and injections were given on alternate days.

The organisms encountered were as follows: the hemolytic streptococcus, 4 cases; nonhemolytic streptococcus, 3 cases; microaerophilic streptococcus, 1 case; anaerobic streptococcus, 1 case; pneumococcus, 7 cases; hemolytic streptococcus and pneumococcus combined, 1 case; and a mixed tuberculous and pyogenic infection, 1 case. In addition there was 1 case of traumatic hemothorax which was sterile.

The penicillin was dissolved in water so that each cubic centimeter of the solution contained 1,000 units. The smallest total amount used was 40,000 units (except in the case of sterile hemothorax, in which 30,000 units were used) and the largest total

amount used was 270,000 units. The number of aspirations and injections varied between 4 and 11.

The patients remained febrile from one week to eight weeks.

Rib resection with drainage, was done in 3 cases because of a bronchopleural fistula, both patients died. Autopsy performed on one of these patients showed empyema, pulmonary and subdiaphragmatic abscesses, fibrosis of the lung and pericarditis.

Of the 16 remaining cases, a satisfactory result was obtained in 5, that is, the patients recovered, without pleural thickening or fibrosis; in the other cases there was either a sterile effusion or more or less pleural thickening and fibrosis. The patient with mixed tuberculous and pyogenic infection became afebrile and the pyogenic organisms disappeared from the fluid.

In a summary of these cases the authors point out that the empyema cavity can be sterilized by the use of penicillin. This however is but one of the objectives in the treatment of this disease; the other is the re-expansion of the lung without fibrosis and pleural thickening, which lead to a reduced vital capacity and the risk of future pulmonary infection. Rib resection is frequently necessary to remove the large masses of fibrin that are present. Before treatment with penicillin is started the sensitivity of the organism should be determined.

FOREST D. DORRIS, M.D.

HEART AND PERICARDIUM

Cornell, A., and Shookhoff, H. B.: Actinomycosis of the Heart Simulating Rheumatic Fever. Report of 3 Cases of Cardiac Actinomycosis, with a Review of the Literature. *Arch. Int. M.* 1944, 74, 1.

Actinomycosis is the most common visceral mycotic infection in man. In about 15 per cent of the cases the infection occurs in the thorax. However in less than 1 per cent of these is there involvement of the heart.

The authors present the case of a thirty-year-old male who was seen because of cough, dyspnea, and weakness for seven months. Precordial pain had been present and severe. Examination revealed some enlargement of the heart to the left with systolic and presystolic murmurs. There was a suggestion of fluid in the right base and marked enlargement of the liver. After about six weeks of observation he became considerably worse and died from what was apparently streptococcus septicemia. Autopsy showed extensive mediastinal adhesions with obliteration of the pericardial sac. A large amount of firm pink, necrotic tissue was present and had invaded the myocardium. The posterior mediastinum was involved by the same process and an esophageal diverticulum was in the mass of scar tissue. Microscopic sections showed the typical ray fungus. The case is unusual in that the symptoms and findings suggest rheumatic fever and in that no external fistulas were present. Review of the autopsy records

In 6 additional cases of actinomycosis revealed that 2 had involvement of the heart

Analysis of these cases and of 65 others collected from the literature shows that the heart may be involved by direct extension of the infection from a neighboring organ or by metastasis through the blood. Metastatic involvement rarely produces clinical signs. About one half of the patients with involvement of the heart by direct extension have clinical manifestations. The most common clinical manifestation in cardiac actinomycosis is congestive heart failure in which the pericarditis plays a major role. The diagnosis can rarely be made clinically.

THOMAS F. THORNTON, JR., M.D.

ESOPHAGUS AND MEDIASTINUM

Collis, J. L., Humphreys, D. R., and Bond W. H.: Spontaneous Rupture of the Esophagus. *Lancet* Lond. 1944 247 179.

Spontaneous rupture of the esophagus after a heavy meal occurred in a man of forty-one years with a previous dyspeptic history. This condition should be kept in mind when doubt is felt about the diagnosis of perforated peptic ulcer. Deep emphysema in the neck is an important physical sign.

Suturing of the tear in the esophagus combined with drainage of the pleural cavity on the affected side offers the best chance of recovery.

Apart from the case reported by the authors, the diagnosis seems to have been made before death on only 3 occasions. The failure to arrive at the correct diagnosis has prevented the institution of surgical

treatment in all except 2 other cases. The present case appears to be the only one in which radical surgical treatment was given to the tear.

PAUL MERRELL, M.D.

Toreson W. F.: Secondary Carcinoma of the Esophagus as a Cause of Dysphagia. *Arch Surg* 1944 38 82.

Twenty-six cases of secondary involvement of the esophagus by cancer are analyzed. Of these 19 cases were encountered among 599 consecutive cases of cancer in which autopsy was performed; an incidence of 3.2 per cent.

Of the 26 cancers 24 were carcinomas, 1 was a lymphosarcoma, and 1 was a cancer of undetermined origin and type, probably a melanoma. The organs in which the tumors originated and the number for each were as follows: trachea or bronchus 8, stomach 7, larynx 4, breast 2, pancreas 2, testis 1, origin undetermined 1. There were 8 instances (about 30 per cent of all cases of secondary cancer of the esophagus) in which the involvement of the esophagus was definitely metastatic from a more or less distant primary tumor.

Among the 26 cases partial or complete obstruction of the esophagus with corresponding clinical symptoms was encountered in 12 cases. In 3 of these cases the involvement of the esophagus was by metastasis from a distant primary tumor.

Secondary carcinoma of the esophagus is not rare and in somewhat less than half the cases leads to more or less dysphagia.

HOWARD A. MCKNIGHT, M.D.

SURGERY OF THE ABDOMEN

ABDOMINAL WALL AND PERITONEUM

Nelson H.: Early Ambulation Following Section of the Anterior Abdominal Wall: An Analysis of 426 Personally Conducted Cases. *Arch. Surg.* 1944 49

Although early ambulation following intra-abdominal operations was first recommended in 1869, the practice has never been generally followed, and most of the few critically analyzed series have been published within the last two or three years.

An analysis of this series of 426 operations through 426 incisions of the anterior abdominal wall after which ambulation was practiced within seventy-two hours shows that the majority of the patients walked on the day of the operation or within the first twenty-four hours.

The incidence of immediate and delayed complications in this series was minimal. Of the 3 partial disruptions of a wound 2 occurred in patients whose wounds had been closed with catgut and for whom early ambulation had not been authorized. The third was due to an error on the part of the surgeon, who failed to order transfusions of blood and plasma for a patient who had lost a large amount of blood. Only 2 incisional hernias, both small, were observed, and there was 1 instance of recurrent incisional hernia in a patient in whom repair was inadequate. The single fatality in the series was due to cerebral thrombosis.

Good results depend on the strict observance of contraindications as well as of indications.

The advantages of the plan include the lower incidence of postoperative complications, particularly pulmonary and vascular complications; the lower incidence of nausea, vomiting and abdominal distention; the earlier return of normal function of the bladder and bowel; the maintenance of normal muscle tone; the psychological effect on the patient's morale and mental status; the acceleration of convalescence and the earlier return of working ability; the economic savings to patient and hospital.

For the reasons stated and because of its apparent absolute safety, the plan of early postoperative ambulation seems to represent a sound surgical advance and its more general employment in properly selected cases is recommended.

JOHN J. MALONEY, M.D.

GASTROINTESTINAL TRACT

De Amnesti, F., and Otis, E.: Cancer of the Region of the Cardia and of the Lower End of the Esophagus (Cáncer de la región del cardia y del extremo inferior del esófago). *Rev. med. Chile* 944, 7

In the series of cases of esophageal cancer here reported the operative technique employed in the

surgical approach to the tumor region was essentially the transthoracic method described by Churchill and Sweet (*Ann. Surg.* 1942 115: 897) and the remainder of the procedure was that described as their own method by Pack and Macner in their collective view on total gastrectomy in the *INTERNATIONAL ABSTRACT OF SURGERY* 1943 77 265. The sub-peritoneal resection of the ninth rib is preferred.

In the preoperative work, special attention is given to the diagnosis and roentgenograms are taken in all possible directions and postures of the patient (Trendelenburg) with thickened shadow media, this to be followed by esophagoscopy and biopsy. Special emphasis is placed on a diet rich in vitamins, carbohydrates and proteins and the hypochromic anemia is combated by saline and glucose solutions and transfusions of blood and plasma.

For the operation preference is given to intubation ether anesthesia variously combined with cyclopropane or nitrous oxide gas. The Levine tube is preferred to jejunostomy and is left lying for from eight to ten days postoperatively before oral feeding is started. Drop-transfusion of blood is carried on during the entire operation.

In the authors' service at the Hospital del Salvador 6 transthoracic explorations have been carried out, with 3 patients limited to simple exploration (no deaths). Of the 3 persons in whom removal of the tumor was decided on 1 died on the ninth day after operation and the remaining 2 have now survived the operation for two and a half months. In 1 instance the spleen was removed with the stomach.

Complete case histories of the 6 patients, all of whom were forty-five years of age or over are appended.

JOSE W. BARRERA, M.D.

Ingelfinger, F. J.: Medical Progress: The Late Effects of Total and Subtotal Gastrectomy. *S. Engl. and J. M.* 944 331 332

Gastrectomy is being performed with ever increasing frequency not only for gastric neoplasms but also in the treatment of peptic ulcers of the stomach, duodenum and jejunum. The reason for this is that resection of the human stomach, particularly of the distal half, has become a practical surgical procedure that carries a remarkably low mortality rate.

In cases of cancer gastrectomy may have to be most extensive, sometimes total. In cases of ulcer the amount of stomach removed varies with the particular problem involved in each instance. Many surgeons recommend the removal of the gastric antrum and at least two-thirds of the stomach, under the reasonable conviction that the chances of a recurrent ulcer are decreased by leaving a gastric remnant that has little or no capacity to form free hydrochloric acid. Indeed the suppression of the normal secretory functions of the stomach is one of the purposes in undertaking a gastrectomy for ulcer.

The question is often asked: Can man live without a stomach or with a stomach whose functions are grossly impaired? The answer is: Yes, but life under such conditions is not invariably normal. The author considers recent evidence bearing on this problem. The present popularity of gastrectomy warrants an appraisal of any possible late effects that may follow total or subtotal removal of the stomach. The immediate postoperative complications are not discussed. So far as possible the author reviews only those effects that can be directly traced to resection of gastric tissue. He asserts that in all probability some of the symptoms for which gastrectomy has been blamed have actually been caused by postoperative ulcer, gastritis or jejunitis. In general he says: "The consequences of removing portions of the human stomach depend on the nature of the primary disease, the extent of the resection, the surgeon's skill and various factors that vary with the patient's age, diet and mental attitude." The majority of the gastrectomy patients find their mode of life unchanged by the fact that half or more of the stomach has been removed.

Certain clinical observations, however, have been noted in the cases of patients who have undergone subtotal or total gastrectomy. About 30 per cent of the patients do not regain their normal weight and some do not regain their preoperative weight. Following subtotal or total gastrectomy about 10 per cent of the patients have an incidence of a persistent postprandial syndrome which follows a fairly typical pattern soon after taking a meal, particularly if the meal is large. There is marked epigastric pressure, distention and fullness. Nausea may accompany these symptoms and occasionally weakness, dizziness, perspiration and palpitation occur within an hour after the meal. In general failure to gain weight is particularly noticeable in the group of patients complaining of gastrointestinal symptoms, but the converse does not hold. Many underweight patients are completely symptom free.

Diarrhea with cramps has been reported as a sequel to gastrectomy, but it is rather rare. Many patients, however, have soft stools following the operation.

Many writers emphasize the fact that the symptoms that can be ascribed to total or subtotal gastrectomy tend to decrease in frequency and intensity as the interval between the operation and the follow-up observations lengthens. Much of the distress present during the first postoperative year tends to disappear subsequently. This improvement is brought about partly by the patient's realization that he must avoid large meals and that he can get along comfortably on six small meals a day. An equally important cause for improvement, however, is the capacity of the gastrointestinal tract to adjust itself to new conditions.

Following subtotal gastrectomy a considerable derangement in gastrointestinal motility ensues. Fluoroscopic observations show that in some instances material leaves the gastric remnant with

difficulty but much more frequently the contrast medium enters the intestine with such rapidity that the term dumping stomach has been used under these conditions. Many modifications of the method of gastric resection have been proposed with a view to lessening subsequent motor disorders. In the European literature a considerable argument has developed concerning the relative advantages of the Billroth I and the Billroth II operations. As yet no conclusive evidence has been presented that one type of operation alters normal gastrointestinal motility less than does another. The gastrointestinal tract makes functional adjustments irrespective of the initial surgery and other factors besides the exact size and position of the stoma influence the rate of gastric evacuation. The gastric remnant, which is at first small, gradually enlarges and resumes some of the reservoir function of the stomach. If the gastric remnant is extremely small, the small bowel dilates to form reservoirs near the anastomosis. The partially resected stomach sometimes exhibits peristaltic waves, but in other cases peristalsis is not seen and the general motility pattern tends to be abnormal. Some investigators, notably Ravdin and his associates, have ascertained that hypoproteinemia is a factor in the retardation of gastric emptying after gastrectomy. Undoubtedly hypoproteinemia can exert a marked influence on motility, but other factors are at work as indicated by the studies of Chauncey and Gray, who could not correlate the level of the serum proteins and the rate of gastric emptying through a stoma. Even if the stoma is anatomically perfect, gastric evacuation after subtotal resection may be delayed by functional disorders. The effect of certain foods on the motility of the upper gastrointestinal tract illustrates the role played by pressure gradients. When fats, hydrochloric acid, or hypertonic solutions enter the intestinal loops distal to the anastomosis, the resected as well as the normal stomach exhibits delayed emptying. It is now known that this delay is produced by relaxation of the gastric musculature, not by sphincteric contraction.

The incidence of functional disorders of gastrointestinal motility after gastrectomy is hard to compute. In the first few months after operation such disorders are doubtless quite prevalent and they as well as mechanical stomal defects should be considered as possible causes of improper gastric evacuation after partial gastrectomy. The edema of hypoproteinemia, if present, may partially occlude the stoma, but it also produces a serious derangement of all gastrointestinal motor functions. With the aid of proper dietary management, functional disorders tend to subside during the first postoperative year and subsequently they are encountered infrequently.

The effects of gastrectomy on absorption have been carefully studied. In gastrectomized patients the glucose tolerance test shows a rapid rise in blood sugar followed by a fall that may reach hypoglycemic levels. In a few cases symptoms occur during the hypoglycemic phase. Carbohydrates and pro-

teins are usually adequately absorbed but some impairment in the absorption of fats may occur.

Pernicious anemia is an extremely rare sequela of gastrectomy. It is quite possible that some of the cases of pernicious anemia associated with gastrectomy are merely due to coincidence. A normochromic or hypochromic type of anemia, however, is not infrequent among patients with gastrectomies.

In general, the outlook following gastrectomy is favorable. A nourishing diet, taken frequently in small quantities and fortified with vitamins and iron often alleviates some of the complications of gastrectomy. Symptoms and various motility disorders, which may be prominent during the first postoperative year subsequently tend to correct themselves spontaneously. Even when the undesirable sequelae of gastrectomy are marked they rarely interfere with the patient's ability to work, and practically never are they so dangerous or distressing as the disease for which the gastric resection was undertaken. Hence the fact that these sequelae may occur can not be considered in any sense as a contraindication to gastrectomy in adults. In the rare cases in which resection has to be considered in an adolescent, it may be wise to limit the extent of the resection.

MATTHIAS J. SEIFERT, M.D.

Hanno, H. A., and Menah M.: Leiomyoma of the Jejunum; Intermittent Melena of Fourteen Years' Duration; and Fatal Hemorrhage. *Ann Surg* 1944 120 99.

The incidence, pathology and clinical features of leiomyoma of the small intestines are reviewed.

The case of a patient with a leiomyoma of the jejunum, who had no known episodes of melena over a fourteen year period and a fatal hemorrhage is reported. It is of interest that ulcer disease, although suspected had never been demonstrated conclusively and that a gastroenterostomy had been injudiciously performed. In all likelihood, had the presence of a tumor of the small bowel been strongly considered and appropriate surgical exploration advocated, the patient might not have died.

This case emphasizes the fact that the presence of small intestinal neoplasms is much too infrequently suspected. The diagnosis of tumors of the small bowel both benign and malignant rests upon a high index of suspicion. The possibility of a neoplasm of the small intestine should be considered in any patient who has repeated episodes of melena in the absence of any demonstrable lesion in the upper gastrointestinal tract or colon, and in any patient with repeated episodes of partial or complete obstruction in the small bowel. In such instances, despite the absence of roentgenological demonstration of a lesion, celiotomy is indicated. Since the ratio of benign to malignant tumors is much greater in the small intestine than in other parts of the gastrointestinal tract, surgery for tumors of the small bowel should on the whole afford a better ultimate result than can be expected for tumors of the esophagus, stomach or colon. CHARLES BAXON, M.D.

Rosin, I. R.: Chronic Bilharzial Appendicitis. *Ca Proc.*, 1944, 3 906.

A brief description of the pathology, history and clinical features of chronic bilharzial appendicitis is given. Although there is still considerable difference of opinion as to whether or not a true chronic appendicitis per se exists from this series it is clear that the pathological entity of chronic bilharzial appendicitis is definitely established and must be borne in mind in the greater part of the entire African continent. Definitely substantiated illustrative cases falling into four different groups are described. These illustrative cases were chosen from 64 cases of definitely established bilharziasis in appendices removed during the past five years. The interesting fact that the urinary infecting agent bacillus haematobium was always recovered from the digested tissues was stressed. The importance of environment in cases of vague abdominal dyspepsia was noted. The overwhelming importance of a routine full histological examination of all appendices removed in the greater part of Southern and Central Africa is strongly urged. All bilharzial cases should be followed up with routine intravenous antimony therapy.

Interesting photomicrographs illustrating the different types of lesions found and described in this series of cases are given. CHARLES BAXON, M.D.

Kaufman, L. R., and Merabheimer, W. L.: Sulfonamides in Appendicitis. A Review of 412 Consecutive Cases and an Analysis of Fatalities. *J Surg* 1944, 65 393.

The oral and parenteral administration of sulfanilamide has been rapidly supplanted by the intraperitoneal application for the more advanced forms of appendicitis. With the intraperitoneal administration the incidence of complications was lower than when only oral and parenteral routes were utilized. Similarly the mortality rate was lower when the sulfonamides were employed intraperitoneally.

The mortality rate is better when no drainage is used. Drainage, however, is indicated when a localized abscess is present, but it adds to the hazard when there is a generalized peritonitis. Again in favor of intraperitoneal sulfonamides is a shorter number of hospital days.

There is apparently little danger of the formation of adhesions from the intraperitoneal application of sulfanilamide powder. However sulfathiazole powder may be a contributing factor according to several observers. Also wound healing may be delayed by sulfathiazole, but not by sulfanilamide.

It is obvious that many factors have contributed an important share to the reduction of the mortality. Among these is the intravenous use of chlorides, plasma or blood to establish optimum fluid balance and the routine use of the McBurney incision, of oxygen, the Wagenseen or Furness suction and the efficient use of the Miller Abbott tube. Since these factors have been brought into play the mortality rate has been reduced. HOWARD A. MCKINNEY, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Walters, W. Watkins, C. H. Butt II R., and Marshall, J. M. Amebic Abscess of the Liver Un-
suspected until Perforation. *J Am M Ass*
1944, 125 963

The authors report 2 cases of unsuspected amebic abscess of the liver which were asymptomatic until sudden perforation of the abscess to the right sub-diaphragmatic region took place. Both patients had been returned to the mainland from naval duty in the South Pacific islands because of a diagnosis of filariasis and lymphadenitis. In neither case was diarrhea present nor were amebae found in the stools. A diagnosis of amebic abscess of the liver was made only after perforation of the abscess to the sub-diaphragmatic region. The similarity of symptoms in both cases was striking after perforation of the abscess occurred. These symptoms were characteristic of amebic abscess of the liver namely chills and fever, lower thoracic and upper abdominal pain, loss of weight and weakness, enlargement of the liver and abdominal tenderness together with a pronounced leucocytosis. There was a sudden development of aching pain in the right shoulder in the right costovertebral region and lower portion of the right thorax which extended to the abdomen with muscle spasm in the right upper quadrant. Roentgenological examinations of the thorax revealed no evidence of pneumonia but showed a progressive elevation of the right half of the diaphragm with an irregular dome-shaped bulge and an increase of the acute cardiophrenic angle to a right angle. There was a variation in temperature daily in both cases of approximately 4° F. In one of these patients the pulse rate increased to a maximum of 140 beats per minute on the day of operation. As a rule the finding of endamoeba histolytica in the stools clinches the diagnosis, however this organism was absent from the stools of both of these patients.

In case 1 the general condition of the patient improved after the administration of emetine 3 gr (0.3 gm.) of emetine hydrochloride were given on the first day 2 gr (0.2 gm.) on the second day and 1 gr (0.065 gm.) on the following four days until a total of 9 gr (0.6 gm.) was administered. Two days following the institution of emetine therapy the patient's temperature returned to normal and varied from 97.5° to 99°F for twelve days. During this time, however the right half of the diaphragm continued to rise progressively because, as was afterward determined, of the increase in size of the sub-diaphragmatic abscess. Open operation was performed and revealed an abscess cavity 10 cm. in diameter in the right lobe of the liver with an opening 3 cm. in diameter into the sub-diaphragmatic abscess cavity. Both cavities contained approximately 1,000 cc. of yellowish white thick, purulent debris with clots of fibrin. Smear and culture showed gram-positive cocci. A strip of iodoform gauze impregnated with sulfanilamide powder was placed in the cavity of

the liver and Penrose drains were placed in the sub-diaphragmatic abscess cavity. Healing occurred in a few days and was followed by complete recovery.

In case 2 there was no apparent response to emetine which had been given at the rate of 1 gr (0.065 gm.) per day on three consecutive days. Since roentgenograms showed a steady increase in the elevation of the right side of the diaphragm a diagnosis of hepatic abscess of unknown origin was made. In view of the extremely serious condition of the patient, the progressive increase in the pulse rate to 140 beats per minute and the temperature of 103.5° F. operation seemed advisable even though there was the possibility of an amebic abscess of the liver with perforation. Surgical drainage was performed as an emergency procedure. A sub-diaphragmatic abscess containing about 240 cc. of typical amebic material was drained through a right sub-costal incision. An abscess cavity approximately 12.5 cm. in diameter was found in the right lobe of the liver by needle aspiration. This cavity was opened and from 500 to 700 cc. of creamy white pus with fibrin and cellular debris were drained out. Smear and culture revealed the endamoeba histolytica. A strip of iodoform gauze impregnated with 5 gm. of sulfanilamide was inserted into the abscess cavity within the liver. This was removed on the twelfth postoperative day after repeated daily soakings with 1:5,000 solution of potassium permanganate. Penrose drains were placed in the sub-diaphragmatic abscess. Complete recovery followed.

Reports such as these lead one to believe that amebiasis is a much more frequent disease than has been commonly supposed. While it is endemic in many portions of the United States and present in all sections the present worldwide dispersal of our armed forces and their subsequent return home will bring about an increasing frequency of this disease. The percentage of cases of amebiasis in which amebic hepatitis or abscess develops is unknown. The avoidance of these developments depends on several factors chief of which are prompt recognition and thorough treatment of the amebiasis. It seems reasonable to suppose that under ideal conditions and if all patients with fresh infections of endamoeba histolytica are promptly and thoroughly treated amebic disease of the liver would not occur since hepatic involvement is always a secondary complication to the disease in the colon. This statement does not mean that every patient who has amebic disease of the liver has a diarrhea or even that he has had diarrhea. It is apparent that many amebic infections of the colon are largely asymptomatic.

MATTHEW J. SWEET, M.D.

Kennaway E. L.: Cancer of the Liver in the Negro in Africa and in America. *Cancer Res* 1944, 4 572

The author has examined the incidence of primary carcinomas of the liver in the negro in Africa comparing it with the incidence of the same lesion in the negro in the United States. He concludes that such

data as are available suggest that the very high incidence of primary cancer of the liver found among negroes in Africa does not appear among negroes in the United States and is, therefore, not of purely racial character. The prevalence of this form of cancer in Africa may be due to some as yet unidentified extrinsic factor. The statistical evidence concerning this question is confused by the inclusion of cancer of the gall bladder in the same category with cancer of the liver.

EARL O. LATIMER, M.D.

Johnson, W., Majstrom, B. L., and Volk, B. W.: A Clinicopathological Study of 100 Cases of Acute and Chronic Gall Bladder Disease. *Ann. Int. M.* 944 31 43.

A study is reported of the case histories of 100 patients who have been operated upon during the last ten years. Calculi were present in 71 patients. Cholecystography showed accurate diagnosis in over 90 per cent of the cases. Among the noncalculous cases, 13 of the patients reported permanent relief, 3 had only temporary relief, and 4 were made worse by the operation. The authors conclude that noncalculous cholecystitis is best treated medically, but when such treatment fails to bring adequate relief cholecystectomy is recommended. In the calculous type surgery is best.

WALTER H. NADLER, M.D.

MISCELLANEOUS

Bulge, R. E.: Experimental Observations on the Human Ileocecal Valve. *Surgery* 944, 6 356.

The authors had the opportunity to make experimental observations on the human ileocecal valve of a twenty-six year-old woman. Their observations were made two months after the exteriorization procedure during a period of four weeks prior to a right hemicolectomy.

The cecum was open, and was attached to the abdominal wall in such a fashion as not to permit encroachment of the parietes upon the terminal ileum or the ileocecal valve. Approximately 10 cm. from the valve the lower ileum was exteriorized and completely cut across so that all intestinal content was evacuated through a proximal external ileal fistula. No intestinal content was transported by way of the distal ileal loop into the cecum.

Qualitative and quantitative control studies of spontaneous activity of the extramural terminal ileum, the sphincter and ileocecal valve were recorded during twenty periods of from thirty to one hundred and twenty minutes each. Additional control records were obtained between the drug experiments.

Control records revealed that there were periods of quiescence and activity in all three areas. The activity of the segments varied, but at times all the segments were quiet. During periods of motility the proximal exteriorized small-bowel loops were equally and similarly active, and expelled intestinal content. At no time was there spontaneous activity in the ileocecal lips, the sphincter or the extramural termi-

nal ileum, independent of activity in the preterminal ileal loops. The extent and frequency of contractions varied, the contractions being most energetic in the morning and less active in the evening. Propulsive activity constituted a small fraction (10 per cent) of the total motility which was nonpropulsive, with varying states of tone. During evacuation at the proximal fistula (usually from two to three hours after a meal) a short comparable period of sphincter and valve motility occurred, which was followed by relaxation of the entire intracecal portion of the terminal ileum.

It was observed that retraction or shortening of the ileocecal structure occurs when the segments are co-ordinated to accept a propulsive wave from an adjacent segment. A nonpropulsive or segmental wave is not associated with shortening of the active segment and the valve is not obliterated.

The author's experimental results indicate that the mechanical, hormonal, and local reflexes of the ileocecal valve and sphincter are so adjusted as constantly to produce responses identical with those of the small intestine to adrenergic and cholinergic drugs. The balloon method of investigation failed to reveal any fundamental distinctions in the behavior of the ileocecal valve, the ileocecal sphincter and the small intestine. The presence of an area of increased contractility was observed within the cecal portion of the terminal ileum. Prolonged tonic contractions, characteristic of sphincter action, were not observed.

JOSEPH K. NARAZ, M.D.

Whitehouse, F. R., and MacMillan, A. M.: Visualization of Rubber Tip of Gastroscope; Differentiation from Gastric Ulcer. *Gastroenterology* 1944 3 23.

The rubber tip of the gastroscope can simulate gastric ulceration.

It is recommended that the rubber tip be colored green or another easily identifiable color to prevent this mistake.

CHARLES BARON, M.D.

Co Tul Wright, A. M., Mulholland, J. H., Canabba, V., and Others: Studies on Surgical Convalescence. Sources of Nitrogen Loss after Gastrectomy and the Effect of High Amino-Acid and High Caloric Intake on Convalescence. *Ann. Surg.* 1944, 30 99.

In a preliminary communication on the subject of surgical convalescence it was reported that patients convalescing from gastrectomy when fed with a high caloric and high amino-acid diet (nutramigen) were able to maintain a consistently positive nitrogen balance throughout the postoperative period, to gain weight, and to achieve an early return to strength, with a significantly shortened convalescence. This was in striking contrast to the response of a similar group of patients under the classical postoperative ward regimen who had a consistently negative nitrogen balance, a loss of body weight, a longer period of postoperative debility and a more prolonged stay in bed.

In the present series of 19 cases, 8 patients were on routine ward regimen, 8 were fed high caloric and high amino-acid mixtures and 3 were fed insufficient quantities to maintain the nitrogen equilibrium.

In the series under the classical ward regimen there was a consistent nitrogen deficit and loss of weight, and a necessarily prolonged stay in bed. Objective ergography showed postoperative asthenia which had not disappeared even on the twelfth postoperative day. In the series of patients who were fed with high caloric and high amino-acid mixtures, there was a consistent nitrogen surplus, a steady gain in weight, and a stay in bed of less than one half that of the control series. The ergograph showed an early return of endurance, on from the fifth to the sixth postoperative day to above that of the initial reading. These findings confirm the results of the preliminary report.

The principal cause of nitrogen loss in postgastrectomy convalescence is the starvation postoperative regimen. Whether there was a larger excretion of urinary nitrogen in the patients in the control group than was present preoperatively is not known.

A hyperalimentation regimen is therefore recommended in routine cases of gastrectomy in order to prevent nitrogen loss, shorten convalescence, and prevent postoperative asthenia.

While the complications in the hyperalimmented group were fewer and less severe than those in the control group, the present series is too small to allow statistically significant conclusions to be drawn from it.

SAMUEL KAHN, M.D.

Presno Albarran, J. A.: Contribution to the Subject of Lumbar Hernia (Contribución al estudio de la hernia lumbar). *Rev. med. ciruj. Habana* 1944 49 53.

No definite operative procedures have been established for the ruptures through the upper lumbar

region as described by Grynfeldt although such hernial predisposition is now generally recognized as being more frequent than that for Petit's triangle; therefore, an operative technique is proposed by this author.

This operation consists essentially in turning for ward as a flap the aponeurosis of this region (through which the hernial sac is passing) tying off and incising the sac, and then sewing the cut edge of the remaining unturned part of the lumbar fascia forward to the base of the flap along the so-called ligament of Henle with mattress sutures; thus the quadrilateral of Grynfeldt is completely closed off. Finally the flap of the aponeurosis of the transversus abdominis is turned back in double-breasted coat fashion and sutured to the fascia covering the erector trunci muscles.

Albarran reports 3 hernias, all of the Grynfeldt type, on one of which he successfully performed his operation. All these hernias occurred in adult males, sixty-four, sixty-two and seventy years old, respectively, all of them were of the acquired type, 2 on the left side, 1 on the right, and all occurred in individuals presumably injured to heavy labor. In no instance was the sac very large or the condition very annoying (2 individuals refused operation). In 1 case the presence in the sac of hollow viscera was evident and the x-rays disclosed an out-sacculution of the colon at the level of the hernial egress.

Incidentally the author reports 2 other cases of hernia at the Garcia Calixta hospital in Havana, which were eventually operated upon successfully by other physicians: one was on a congenital basis in a female infant of seven and one-half months; the other in a white male seventy years of age and had been diagnosed as tuberculous peritonitis. The hernia in this case had been mistaken for a cold abscess (incision, fecal fistula).

JOHN W. BRENNAN, M.D.

GYNECOLOGY

UTERUS

Bickera, W.: A Study of the Endometrial Pattern Before and After Treatment for Amenorrhoea. *Am. J. Obst.*, 1944, 48, 58.

This study is based on the observations made upon 9 women whose chief complaint was secondary amenorrhoea. The term secondary amenorrhoea was limited to those patients in whom there had been a cessation of menses for a period of five months or more. The patients with amenorrhoea are divided into two groups according to the endometrial pattern which the patients show.

Repeated endometrial biopsies are taken at weekly intervals to establish the endometrial type.

When a persistent proliferative phase of endometrium is found at successive weekly biopsies this indicates a failure of ovulation and, therefore, a pituitary-ovarian defect. The finding of a persistent secretory endometrium at successive biopsies suggests the influence of a persistent corpus luteum.

Seven of the 9 patients had a persistent proliferative phase (anovulatory) endometrium. The endometrium varied from a very atrophic type with scarcely any glandular structure to marked hyperplasia. Although the 7 amenorrhoeic patients showed a wide variation of endometrial pattern, the pattern in any 1 case was extremely constant.

When weekly biopsies were taken of these patients it was found that there was an amazing persistence of the endometrial pattern in each individual patient.

The pathological physiology involved in anovular amenorrhoea is thought to be the result of a pituitary ovarian failure primary or secondary to some systemic disease.

Treatment consisted in the stimulation of uterine bleeding by the sudden withdrawal of estrogen progestosterone to a lower level in an attempt to simulate the normal physiology of the body and thus induce normal uterine bleeding. After the patients had been adequately studied by means of successive biopsies they were given stilbestrol, 5 mgm. daily at bedtime for ten nights. On the last five days of the stilbestrol therapy, it was supplemented by progestosterone, 5 mgm. daily given intramuscularly. Following this intensive ten-day therapy, uterine bleeding occurred in 6 of the 7 patients within four days. The average duration of the induced menstruation was three and one-half days. One patient with marked atrophy of the endometrium failed to menstruate. In the 6 successful patients the ten-day course of treatment was repeated on the fifteenth day from the first day of the induced bleeding. Five of the 6 patients had another episode of uterine bleeding within fifteen days after completing the second course of therapy. No further treatment was given. Of the 5 patients in whom a second bleeding phase was induced all continued to menstruate at fairly regular

intervals for periods of seven, three, twelve, one, and twelve months, respectively without further treatment. Of these, 3 lapsed into their original amenorrhoeic state when treatment was stopped, but only after three and nine months of spontaneous menstruation respectively.

Two of the 9 amenorrhoeic patients were found to have a persistent secretory phase endometrium.

Case No. 8 showed no pelvic pathology and the ovaries were normal to palpation. Endometrial biopsy showed a persistent secretory phase. Despite a negative pelvis, the diagnosis of persistent corpus luteum was made and a laparotomy performed. At the operating table the ovaries were smooth and of normal size, with no follicle cysts. Incision depicts the right ovary exposed a healthy glistening yellow corpus luteum approximately 1 cm. in diameter. This was excised and menstruation followed on the second day and recurred at from twenty-seven to thirty-one-day intervals until the patient became pregnant, after a six year sterility.

Case No. 9 was treated as a sterility study and menstruation ceased for three months. The Friedman test was positive. The patient was followed for two more months, during which time the amenorrhoea persisted but the uterus did not enlarge. A soft doughy mass was palpable in the region of the left ovary. It was estimated to be 9 cm. in diameter. Repeated endometrial biopsies revealed a persistent secretory phase of endometrium. The patient was operated on and a corpus-luteum cyst of the left ovary 6 cm. in diameter was removed. Thorough curettage failed to reveal chorionic villi. The patient menstruated normally on the third postoperative day and a normal cycle has occurred since.

HENRY C. FALK, M.D.

ADNEXAL AND PERIUTERINE CONDITIONS

Lesh, R. E.: Torsion of Ovarian Cysts in Children. *Am. J. Obst.*, 1944, 47, 845.

Torsion of ovarian cysts in young children is a rare occurrence. The author reports 2 cases: one a simple cyst in a child of four and the second a dermoid in a twelve-year-old girl. It is suggested that the presence of a cyst be considered in any child complaining of abdominal pain. Surgical removal is indicated.

J. ROBERT WILLIAMS, M.D.

Schwartz, F. L.: Salpingitis and Tubal Patency. *Am. J. Surg.*, 1944, 64, 65.

In determining tubal patency hysterosalpingography when properly done even in the presence of salpingitis, carries no more risk than any other diagnostic procedure. While it may lead to more possible complications, the morbidity is negligible, and the procedure is superior to gas insufflation from both diagnostic and therapeutic standpoints.

In the presence of salpingitis of sufficient duration and severity to warrant surgery but in cases in which preservation of child bearing function is desired this procedure is of value for deciding between continued local treatment and surgery.

A series of 165 patients was reviewed. The roentgenographic findings were compared with the surgical and pathological pictures. There were 12 pregnant patients and 18 on whom bilateral salpingectomy was done. In all those coming to surgery, definite tissue changes were found and all patients were free from symptoms after surgery.

Salpingitis may be present even though a tube is permeable. Such tubes present certain characteristic roentgenological features such as elongation, clubbing and redundancy at the extremity as well as areas of stenosis and dilation. Pregnancy is rare in this type of tube in spite of its permeability.

Occlusion at the cornu prevents reinfection from below and, as a general rule, results in self-sterilization and healing of the tubes.

There were 29 women with both tubes completely patent who had entirely negative histories and findings. Disturbances of ovulation were quite frequent and there was only 1 pregnancy in the group.

Seventy four patients had both tubes patent but some history of salpingitis. In this group the tubes were listed as patent provided they were permeable to oil even though there was evidence of partial obstruction. From serial films it appeared that many of these tubes had been opened by pressure of the oil. Nine of these patients became pregnant and 7 were subjected to surgery.

Of 5 patients with one tube patent and the other blocked at the cornu and with negative histories and findings 2 became pregnant.

Twenty-one women had one tube blocked at the cornu with symptoms on the patent side. There were no pregnancies and 7 women required surgery.

With one tube blocked at the cornu 4 patients had bilateral symptoms and 1 patient presented symptoms on the same side. One patient had one tube patent and the other blocked at the isthmus following removal of a large ovarian cyst.

Five women had one tube blocked at the fimbriated extremity 1 of these required surgery.

Of 11 patients with both tubes blocked at the cornu 10 were well and one was well after operation.

Two patients had both tubes blocked at the isthmus. One had a bilateral hemisalpingectomy previously and is well the other had mild recurrent salpingitis.

Eight women had one tube blocked at the cornu and the other blocked at the fimbriated extremity.

Five were free from symptoms and 2 of the 3 with symptoms required operation.

Four patients had both tubes blocked at the fimbriated extremities 3 are well and the fourth had a bilateral salpingectomy.

The not infrequent roentgenological findings of tubal damage in young women with completely negative histories and tubal findings suggests the possibility that the vague lower abdominal pains often complained of during childhood and adolescence may be the result of an unrecognized blood or lymph borne salpingitis.

In a number of cases with a record of previous varied treatments symptoms have been relieved by hysterosalpingography.

Tubal patency can be and often is coincidental with salpingitis, although in the majority of such cases the tubes are not completely patent. Cornual occlusion usually results in self-sterilization and self healing.

CHARLES BARON, M.D.

MISCELLANEOUS

Finkler, R. S. Zondek's Simplified Treatment of Secondary Amenorrhea. *Am J Obst* 1944 48: 26.

A series of 31 patients with secondary amenorrhea due to pituitary or ovarian deficiency is presented and the results with the simplified two-day treatment are described.

This method devised by Zondek consists of the injection of a combination of estradiol benzoate (2.5 mgm.) and progesterone (12.5 mgm.) on two consecutive days. Uterine bleeding was produced in 25 patients (80.6 per cent). Among the 6 patients who did not react were 4 with marked uterine hypoplasia. In 2 of the unresponsive patients the amenorrhea had persisted for more than two years. By restricting the simplified treatment plan to patients with an amenorrhea of less than two years duration the percentage of favorable responses can probably be further increased. No marked changes were produced in the endometrial pattern with the two-day treatment as evidenced by the pre- and postmedication biopsy specimens.

The advantages of the simplified method are discussed. The two-day treatment plan should be employed in all those instances of functional amenorrhea of less than two years duration in which thyroid medication has failed to yield results, and in which for some reason or another it is desirable or imperative to obtain uterine bleeding in as short a period of time as possible.

EDWARD L. CORNELL, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Sontag, L. W. Reynolds, E. L., and Torbet, V.: The Relation of Basal Metabolic Gain During Pregnancy to Nonpregnant Basal Metabolism. *Am. J. Obst.* 1944 48 315

The explanation of the changes in the metabolism during pregnancy may lie in the effect of the fetal thyroid on the hypothyroid mother. It is possible that the physiological changes of pregnancy provide a resurgence of function of the maternal thyroid. In the Fels nonpregnant series, 44.8 per cent of the women had basal metabolic rates below 10 per cent on the basis of the Mayo Clinic standards. Basal metabolic rates during the ninth month of pregnancy were preponderantly at the level which would usually be considered normal for nonpregnant women. These facts can probably be explained on the basis of differences in the conditions under which the basal metabolism is measured. The low basal metabolic rates observed in the Fels series were compared with Davis Milwaukee and Wilmington series which also showed low values. The possible need for interpretation of test results in terms of the environment, the significance which the patient attaches to the test, the general anxiety and the previous test experience is suggested.

EDWARD L. CORNELL, M.D.

Didle, A. W.: The Effect of Travel on the Incidence of Abortion. *Am. J. Obst.*, 1944, 48 354.

Ninety-eight and one-tenth per cent (1,038 cases) of the patients considered were under observation to the end of the third month of pregnancy, while 91.5 per cent (968 cases) were followed up beyond the fourth month. All of the abortions seen occurred before the end of the third month with the exception of 8.

During the period of scientific scrutiny a diagnosis of abortion was made and proved anatomically 123 times, or an incidence of 11.6 per cent. Three individuals were seen through 2 each. Of the 123 23 were dropped from the study because there was no information on travel. In the final analysis, there were 239 travelers and 467 "nonjourney" women for the first sixteen weeks under study.

Among the 446 women with complete data, 215 took no trips 179 traveled from 70 to 6,000 miles each in a continuous tour by bus and/or car and/or train before the end of the fourth month and 53 covered from 170 to 4,000 miles each after this period of time. Repeated trips averaging 1,000 miles were again made by 30 of the 179 patients after the fourth month. The distribution by state, age of the patients, blood counts and body weights were approximately equal for the different groups. The abortions predominated in the second month (51 cases) with 41 in the third, and 8 in the fourth.

Consideration may now be given to the problem of travel and abortion. Of the 239 travelers who toured before the end of the fourth month, 16 (6.6 per cent) had untimely births as contrasted to 11 (17.9 per cent) among the control or sedentary series. Among the 179 protocols for which the distances covered were known definitely 46 (25.7 per cent) of the women were multigravidae and 37 (20.6 per cent) parous. These figures correspond favorably with the percentages for the entire clientele. Of the 16 "journey" women having abortion difficulties, 7 were parous and 1 other was gravid previously. The remaining 8 were primigravidae.

Up to the present time, statements have been made in the literature cautioning pregnant patients against travel, but in so far as clinical data are concerned, material to substantiate these cautions is all.

Formerly when women became pregnant, the majority stayed near home and abstained from taking extended trips. As a result, no one physician or clinic had the opportunity of reviewing the results of travel on the incidence of abortion in a relatively large number of cases. Today the means of transportation are so modernized that they do not lead themselves well to the evaluation of the abnormalities, if any produced by rough riding.

EDWARD L. CORNELL, M.D.

LABOR AND ITS COMPLICATIONS

Roberts, P. G.: The Use of Methergine (Syntetic Ergonovine) in the Third Stage of Labor. *Bull. J. Surg.* 1944, 52 380.

Kirchhof and others of the University of Oregon, Department of Pharmacology studied the oxytocic activity of methergine on the uterus and on the sympathetic nervous system. Their experiments showed that, in the guinea pig or the rabbit, methergine was equal or superior to ergonovine in activity. Fetal toxicity could not be demonstrated in small animals in the doses employed.

Stoll and Hofmann described methergine as α -hydroxy acid- β -hydroxybutylamide. Methergine was administered intravenously in doses of 1 cc. containing 0.5 mgm. of lysergic acid- β -hydroxybutylamide-2 to 34 patients (6 primiparas and 28 multiparas) in the third stage of labor. Immediately after delivery of the infant a 1 cc. ampule of methergine was given intravenously. With the first change of the uterus to firmness (usually within from twenty to thirty seconds) expression of the placenta was attempted. Spontaneous expulsion into the vagina was a common occurrence. Expression was usually accomplished by compression of the anterior and posterior surfaces of the uterus without downward pressure of that organ into the pelvis.

The method for measuring blood loss was as follows:

Immediately after delivery of the baby an oil-silk drape was placed under the buttocks of the patient and a fresh pan was placed on the floor. In cases in which episiotomies were done the drape was pinned to the perineum above the incision to form a trough for the reception of uterine blood which was measured carefully.

The average loss of blood in the patients who had received methergine was 181 cc. and the average loss in the control series was 247 cc. A blood loss of less than 500 cc. occurred in 93 per cent of the women who had received methergine a very favorable figure compared with 75 per cent of the control series. A severe hemorrhage of 850 cc. of blood occurred in 1 case (2.94 per cent of the patients) in which the drug had been given but the greatest corresponding loss in the control series was 1,200 cc. (7.66 per cent).

Certain factors are of utmost importance for the reduction of blood loss when an oxytocic preparation is used intravenously in the third stage of labor viz.

1. Immediate uterine massage after the drug is injected—from twenty to thirty seconds.

2. Immediate expression of the placenta as soon as the first contraction is felt after intravenous injection. The operator must keep his hand constantly on the fundus in order to detect that contraction.

A marked shortening of the third stage of labor was characteristic of the cases receiving methergine. The response to natural ergonovine was weak in comparison with the rocklike firmness of the fundus after the administration of methergine. Furthermore this hard contraction was maintained for a long period of time.

In cases of cesarean section, the surface of the uterus becomes mottled with paler and darker areas the entire fundus shrinks in size and bleeding becomes minimal. After this reaction has been observed it is not surprising that in the normal delivery there is prompt separation of the placenta with almost complete cessation of bleeding.

In 83 per cent of the patients receiving methergine the third stage of labor lasted five minutes or less. It is the author's belief that if the placenta has not been delivered within twenty minutes after the intravenous administration of an ergonovine preparation it should be considered a retained placenta and steps taken to deliver it by manual extraction should a contraction ring be forming.

The reaction time averaged thirty seconds, although in many cases it was only ten seconds. The fundus remained in a remarkably hard state for several hours. In all cases, contraction of the fundus following the administration of methergine was stronger and of considerably greater intensity and duration than with the usual ergonovine preparations. If there is much delay between the time of drug administration and the attempt at placental expression the incidence of lower uterine contraction ring with the danger of retention of the placenta is increased.

In both the methergine group and the control group there was 1 case of partially retained placenta.

DANIEL G. MORTON, M.D.

Mendelson C. L.: The Management of Delivery in Pregnancy Complicated by Serious Rheumatic Heart Disease. *Am. J. Obst.* 1944 48 339

A series of 1,089 patients with pregnancy complicated by rheumatic heart disease is presented. This complication occurred in 2.6 per cent of 41,459 pregnancies. The functional-capacity diagnoses according to the New York Heart Association criteria, were 480 (44 per cent) class 1, 1,443 (41 per cent) class 2, 113 (10 per cent) class 3, and 54 (5 per cent) class 4.

The total mortality was 11 (1 per cent) and the cardiac mortality 8 (0.7 per cent). All cardiac mortality was due to decompensation—5 patients died undelivered and 3 died after abdominal delivery.

The class 3 and class 4 cases are completely analyzed. Twenty-six of the patients were delivered abdominally with 3 deaths (12 per cent) and 136 were delivered vaginally with no deaths.

The abdominal group consisted of 5 hysterectomies with 1 death, and 21 cesarean sections with 2 deaths.

The vaginal group consisted of 35 abortions and 107 viable deliveries. Cardiac failure occurred after the fourth month and death occurred in 15 per cent of these cases.

An outline for the management of pregnancy complicated by serious rheumatic heart disease, (class 3 and 4 cases) is presented. The successful management of pregnancy complicated by serious rheumatic heart disease requires a program of medical and surgical obstetrics of the highest order.

In the absence of other obstetric complications the vast majority of patients can be successfully delivered by the vaginal route. When indicated vaginal therapeutic abortion is a relatively safe procedure for the interruption of early pregnancy.

The hazards of labor can be definitely reduced with good antepartum care, careful functional evaluation, adequate digitalization, and shortening of the second stage. The pulse and respiratory rates intrapartum provide a valuable guide to the cardiac status. Abdominal delivery has been performed with decreasing frequency yet it may still have its place for those cases which fail to improve in spite of treatment.

Each patient should be evaluated as an individual problem. Once severe cardiac failure has occurred antepartum, there is a great risk in discharging the patient from the hospital before delivery.

The incidence of spontaneous abortion and premature labor, the duration of labor and the blood loss at parturition in women with serious rheumatic heart disease are not significantly different from these values in normal women.

EDWARD L. CORNWELL, M.D.

Briscoe, C. C.: Cesarean-Section Morbidity and Septic Mortality in Relation to the Type of Operation. *Am. J. Obst.*, 1944 48 16

Septic infection notably peritonitis holds an enviable position as chief of the causes of death fol-

lowing abdominal delivery, accounting for 36.3 per cent of the deaths in Philadelphia in 1941.

The author reviewed all cesarean sections performed at the Philadelphia Lying in Hospital during the past three years. During this period there were 409 cesarean sections performed by 59 operators with 3 deaths, or 0.7 per cent.

Cesarean section performed before labor begins offers the patient the most protection against sepsis.

Postcesarean morbidity rates at the Philadelphia Lying in Hospital during the past three years show superiority of the low section over the classical for the elective case and especially during labor.

Over a third of the women who die in Philadelphia following cesarean section die of sepsis. One half of the deaths occurred in patients who had been in labor over twelve hours before operation. 37 per cent of whom showed signs of sepsis preoperatively. The absolute death rate and the relative death rate from sepsis show superiority of the low operation for the elective case and especially for the patient in labor.

The supposed protection of the Porro operation for the infected patient has been lacking in Philadelphia during the past twelve years.

Reported series of extraperitoneal operations show the death rate from all causes to be from two to five times less than the death rate from sepsis alone for the Porro operations performed in this city.

The operation of choice for the infected patient would seem to be an extraperitoneal cesarean section.

EDWARD L. CORNELL, M.D.

PURPERIUM AND ITS COMPLICATIONS

Rotstein M. L.: Getting Patients Out of Bed Early in the Puerperium. *J. Am. M. Ass.* 1944 13 838.

A series of 150 uncomplicated obstetrical cases were selected at random for the purpose of studying the effects of getting patients out of bed early in the puerperium.

From the historical viewpoint, prolonged bed rest was preferable because of the fear of uterine prolapse. Observations during the period from 1940 to 1941, in London, showed no ill effects as a result of mobilizing puerperal women early.

Of the group observed, 65 were primiparas and 85 were multiparas. Delivery was spontaneous in 51; low forceps were used in 85 deliveries and mid forceps in 8; the remaining 6 were breech deliveries. Episiotomy was done in 117 patients.

Routine management of the patients selected for study was as follows:

1. Immediately after delivery the patient was encouraged to move about in bed.

2. Ergonovine hydrochloride (1/320 gr. or 0.3 mgm.) was given to each patient every four hours for six doses.

3. The patient was catheterized every ten hours if unable to void but no antiseptic solutions were instilled.

4. Routine perineal care was instituted. This consisted of flushing the perineum with sterile water after micturition and defecation.

5. The patient was put on a full diet immediately.

6. Liquid petrolatum was given on the night of the third day.

7. Starting on the third day each patient was made to lie on her abdomen for one hour.

8. A soap-suds enema was given on the fourth morning.

9. On the morning of the third or fourth day if the four-hourly oral temperature had not been above 99.6°F for the preceding twenty-four hours, the patient was allowed up in the chair for two hours, and again for two hours in the afternoon. Forty-five patients or 30 per cent were first allowed up on the third postpartum day and 105 or 70 per cent, on the fourth postpartum day.

10. On the fifth postpartum morning each patient was allowed to walk about as she desired, and she continued to do so until the day of her discharge.

11. Starting on the fifth postpartum day each patient was put in the knee-chest position for twenty minutes. This procedure was carried out each day until discharge of the patient, and its continuance for two weeks, at home, was prescribed.

There were no serious complications in the entire series. The patients felt better and stronger than patients who had not left their beds early and they were able to care for themselves equally as well as the patients who had been confined to bed. An increase in the amount of lochia occurred on arising, but involution occurred more rapidly and morbidity was not increased. Three patients had postpartum bleeding after they had been discharged from the hospital. Uterine retroversion was encountered less frequently than was expected under the usual postpartum management. Prolapse did not occur. Episiotomy wounds healed without difficulty and the patients were more comfortable out of bed. No venous complications occurred. JAMES F. DOXON, M.D.

González, J. B.: Severe Puerperal Fever: the Puerperal Fever of 1921, and Puerperal Fever at the Present Time (La fiebre puerperal grave, la fiebre puerperal de 1921 y la fiebre puerperal de ahora). *See med., B. Air.* 1944, 41, 2.

The author discusses a term introduced comparatively recently into gynecological terminology namely that of "severe puerperal fever" and calls upon those who use it to explain in what way this severe puerperal fever differs from ordinary puerperal fever. He declares there is no difference in bacteriology, pathological anatomy or any clinical difference. The severe cases are ones that have been allowed to become severe by the use of mistaken treatment.

In 1921 he published his first statistics from the obstetric department of the Hospital Teodoro Alvarez in Buenos Aires. There was no mortality in his cases of puerperal fever. Objections were made to his findings and he invited his colleagues to come in and observe his cases and the results. Only one accepted

the invitation and he was obliged to confirm the author's findings.

Puerperal fever is an infection of the genital canal which occurs following delivery the infection being caused by one or several of the ordinary pyogenic cocci. All cases can proceed to normal recovery if the author's strictly abstentionist treatment is carried out. The patient is kept in the best possible general condition no examinations are made of the genital canal and the position is such as to allow free discharge of all lochia from the vagina. There may be a daily gentle cleansing of the vulva with a sponge wet with hydrogen peroxide and blood transfusions suffice to stimulate the defensive forces of the body.

Four cases are described which support his theory. They might be called severe cases as the course was prolonged and one patient had a septicemia and another a thrombophlebitis. The patient with septicemia died, the only fatality in the author's clinic. However the patient had been brought in five days after delivery with a retained placenta.

AUDREY G MORRIS, M.D.

MISCELLANEOUS

Cameron C. S. and Graham S.: Antenatal Diet and Its Influence on Stillbirths and Prematurity. *Glasgow M J.*, 1944 143 1

A record was made of the food intake of 300 mothers—100 mothers of still born infants, 100 mothers of prematurely born infants and 100 mothers of normal full time infants. There was no selection of cases in any way and obstetrical causes were not considered. The standard of prematurity was the usually accepted one, namely an infant with a birth weight of 2.5 kg or under. The investigation was made after the confinement and before the mother left the hospital but covered the last three months of pregnancy.

The diet of each of the 300 mothers was then recorded in terms of intake of calories, carbohydrate, fat, protein, calcium, phosphorus and iron. The average amounts of each of these constituents together with the optimum requirements for expectant mothers, are given in Table I. The vitamins were not considered in this study although their importance must not be overlooked.

TABLE I.

	Optimum requirements	Stillbirths	Premature births	Full-term births
Calories	2,500	1644	1710	1946
Carbohydrate (gm.)	350	207	217	217
Fat (gm.)	80	61.9	64.9	80.4
Total protein (gm.)	90	53.4	54.5	73.1
First-class protein (gm.)	50	27.4	29.9	45.9
Calcium (gm.)	1.5	0.76	0.8	1.22
Phosphorus (gm.)	2.0	0.91	0.95	1.37
Iron (mgm.)	15.0	9.0	9.0	11.0
Age		32.1	28.4	28.6
Parity		4.2	2.9	3.13

Scrutiny of the group values indicates the superiority of the diets of the mothers with full time infants in every respect but relatively this is most noteworthy as regards first class protein, calcium and phosphorus, for which the figures for the two other groups are less than two-thirds of those for the mothers with full time infants and of the optimum values. The diets of mothers of still born and prematurely born infants show remarkably little difference from one another. There is a consistent but very slight difference in favor of premature births in respect only of proximate principles, but none in mineral values. Statistical analysis of the figures indicates that the superiority of the diets of the mothers of full-time babies is definitely significant but that the minor differences between the diets of the other two groups are quite unsubstantial, statistically or otherwise.

To test the validity of these findings in a practical way it was decided to supervise the diets of a certain number of expectant mothers and compare the results of their pregnancies with those of a control series. Accordingly, the diets of 500 women attending the antenatal clinic at the hospital were supervised during the last three months of pregnancy.

To serve as a control the records of 500 women attending the antenatal clinic during the same period but whose diets were not supervised were used. The findings are recorded in Table II and as far as they concern stillbirths and premature births are regarded as significant.

TABLE II

	Supervised group	Control group
Stillbirths	21	36
Premature births	51	50
Neonatal deaths (in hospital)	8	10
Infants breast fed on dismissal from hospital	357	276
Average parity of mothers	2.96	3.08
Average age of mothers	28.38	28.8

The results in the present investigation show the relative superiority of the diets of the mothers who bore full term infants. Confirmation of these results was obtained in practice. When the diets of the expectant mothers were improved by instruction and encouragement given at an antenatal clinic by a trained dietician the incidence of stillbirths and premature births was reduced. The results of the second part of the investigation may be taken as indicating the minimum amount of improvement which might be expected if the diets of the expectant mothers were increased to the optimum.

CHARLES BARON, M.D.

Hoenig, E. and Warner, M. P.: Full Term Pregnancy After Removal of the Remaining Ovary at Five Months of Gestation. *Am J Obst* 1944 48 431

The authors report a case of a full-term pregnancy in a patient possessing only one ovary after removal of the remaining ovary at five months of gestation. The

patient was a twenty-seven-year-old para-0 who had had one ovary removed three years before the present pregnancy. During the course of this pregnancy she was admitted to the hospital at the fifth month complaining of severe abdominal pain. A diagnosis of twisted ovarian cyst was made and at operation the remaining ovary was removed.

In spite of the removal of the only ovary and the corpus luteum of pregnancy, this patient continued in her pregnancy uneventfully and delivered a normal infant without incident.

This is another case to prove that the ovaries are not absolutely necessary for the successful continuation of pregnancy after the fourth or fifth month of gestation.

HARRY FIXLER, M.D.

Eastman, N. J.: The Abuse of Rest in Obstetrics
J Am Med Ass 1944, 135: 1077

The abuse of rest in obstetrics is discussed in relationship to the employment of pregnant women in industry and to the deep-rooted teaching of child spacing.

On the basis of the large number of women employed in industry at the present time it is estimated that a minimum of a quarter of a million of these become pregnant every year. Government agencies and the Committee on Health of Women in Industry of the Section on Obstetrics and Gynecology of the American Medical Association are agreed that pregnant women can be employed in industry with safety. Adequate antepartum care and rest periods are essential. Jobs requiring night work, heavy lifting, prolonged standing or having a good sense of bodily

balance should be prohibited. A minimum of six weeks leave before delivery should be granted. Experience in Britain during the present crisis confirms the feasibility of employing pregnant women.

Many employers now discharge women when pregnancy is discovered. Because of this, attempts are made to conceal the pregnancy early prenatal care is avoided and many women seek the aid of the criminal abortionist. As a consequence an unhealthy attitude toward maternity is acquired and the use of contraceptives is compulsory.

The second abuse of rest is associated with child spacing. It has been axiomatic for many years that an interval of two years should elapse between pregnancies. A previous report by this author showed this to be untrue. His conclusions were:

1. There is no appreciable increase in the rate of stillbirths or neonatal deaths when the interval is less than two years.

2. Hypertensive toxemia is least frequent when the interval between the first and second pregnancy is less than two years, increased when between two and four years, and greatly increased when over four years.

3. In the event of previous hypertensive toxemia, the likelihood of repetition is increased the longer the interval.

4. The incidence of premature labor, anemia, postpartum hemorrhage, and puerperal infection was not increased by intervals of less than two years.

5. There was no difference in the ability to nurse.

6. The weights of the mature babies was approximately the same.

JAMES F. DOUGHERTY, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY AND URETER

De la Peña, A. and De la Peña, E. Case Report Illustrating Brief Period of Time Necessary to Formation of Large Staghorn Renal Calculus. *J Urol* Balt, 1944 52 108

A case is reported of a thirty-seven year-old female who had a nephrostomy of the kidney on the left side a year before the authors saw her. A urinary tract roentgenogram at the time the authors saw the patient revealed 2 small stones in the left renal area, and the patient complained of colicky pain in the left renal area as well as in the right iliac fossa. A month after this film was taken the patient was seized with right lumbar colic and fever. A film at this time (thirty-eight days after the first) demonstrated the perfect mold of a large stag horn calculus filling the right renal pelvis. Operation was refused. Following this the patient suffered right lumbar pain and fever and passed small calculi. The left kidney was found to be nonfunctional nine months later and the right partially so. At this time operation disclosed the left kidney to be merely a functionless pyonephrotic sac.

Two months later the patient suffered right lumbar pain and a plain roentgenogram demonstrated no appreciable change in the size of the right stag horn calculus as visualized nine months earlier. This stone was removed by nephrolithotomy. The kidney was found sclerotic in the upper pole and the secreting tissue was confined to the lower pole. This was less than a third of the kidney mass. The patient's postoperative course was uneventful.

The case is recorded since here a large renal stag horn calculus of no more than thirty-eight days incubation was observed and the size of the stone was unaltered at operation nine months later.

ROBERT LICH, JR. M.D.

BLADDER, URETHRA, AND PENIS

Mueller, S. R. and Hamilton, J. B.: The Effect of Testosterone Propionate on the Tonus of the Urinary Bladder. *J Urol* Balt, 1944, 52 139

Cytometric studies designed to determine whether or not the tonus of the bladder may be influenced by androgenic treatment were carried out in 6 men and 2 women. The intravesical pressures observed with the introduction of increasing amounts of fluid into the bladder were higher in all of the men and in 1 of the women following treatment with male hormones. There was an increase in the maximal intravesical pressure developed both before pain or discomfort was first noted and before the pain was sufficiently severe that the test was terminated. The volumes of fluid contained in the bladder at the first appearance of pain and at the onset of severe pain were similar to or slightly smaller than those

that produced similar phenomena prior to medication. In most instances the intravesical pressure at which the first desire to void was experienced was increased upon androgenic treatment, but the volume of intravesical fluid at this point did not vary in a uniform manner.

This augmented tonus of the musculature of the bladder that accompanied androgenic treatment was much in excess of the normal range of variability and could not be accounted for by technical procedures. Neither the increased tonus nor an apparent improvement in control of micturition are attributable to change in prostatic size or consistency.

JOSEPH A. LOFF, M.D.

Pole, F. Recurrent, Nontraumatic Rupture of the Urinary Bladder—a Case Report. *Virginia M Month*, 1944 71 477

The gravity of urinary vesical rupture is emphasized by referring to Campbell's report which showed that from 60 to 80 per cent of the patients with this condition died. It was Campbell's conclusion that delay in treatment and infection of the urine were the most prominent factors influencing the mortality. Hence early operation and the institution of free drainage are paramount in bladder rupture.

The author reports a case of a recurrent non-traumatic rupture of the bladder in a thirty-two-year-old colored male who had a previous history of urethral obstruction with trocar drainage of the bladder seven years previously. During the intervening time the patient was treated for penurethral abscesses and in 1942 an intraperitoneal pelvic abscess due to vesical rupture was drained but cystostomy at that time was deemed impossible because of peritoneal adhesion of the intestine to the anterior surface of the bladder.

On admission in 1943 in view of the patient's past history, and in addition his complaint of severe low abdominal pain of three days duration oliguria, chills fever and generalized abdominal rigidity a diagnosis of vesical rupture was made. The total white blood cells were 20,100 with 92 per cent of polymorphonuclear leucocytes.

At operation the diagnosis was confirmed. Generalized peritonitis was present with free pus in the abdominal cavity. The bladder was found thick and inelastic with a 0.5 cm. opening of the peritoneum communicating with the bladder lumen. The opening was closed with catgut, the purulent fluid was aspirated, sulfanilamide and sulfathiazole powder was implanted in the abdominal cavity and a penrose drain was inserted to the point of vesical rupture. The bladder was drained suprapubically through a separate stab wound. At a later date the urethral strictures were excised, and the patient was discharged from the hospital with a urethral caliber of 22 F.

ROBERT LICH, JR., M.D.

Hatch, W. E., and Wells, A. H.: Actinomycosis of the Urinary Bladder Complicating a Case of Madura Foot. *J. Urol. Balt.*, 1944, 33: 149.

A case of actinomycosis of the urinary bladder which was apparently secondary to a long-standing actinomycosis of the foot and lower leg has been reported, with autopsy findings.

The only important autopsy findings were in the kidneys, urinary bladder and right lower leg and foot. The perineal fat was unusually adherent, but the capsule could be stripped from the kidneys without difficulty. Outer surfaces of the kidneys were finely granular. The kidneys weighed 145 and 160 gm. The parenchymal tissue was unusually pale and somewhat flabby. There was a very slight bilateral hydronephrosis and hydroureter. Microscopic sections of the kidneys revealed approximately grade II patchy interstitial fibrosis and lymphocytic infiltration without thickening of the artery walls. There was no frank granulation tissue or abscess formation in the kidneys. There was no infection or thickening of the walls of the pelvis or ureters. The bladder wall was from 8 to 10 mm. in thickness and was fibrous in nature. The bladder contained about 400 cc. of dark-red, tenacious blood clots. A few tiny blood clots were attached to the bladder wall. The mucosal surfaces were relatively smooth throughout. There were areas of superficial erosion with small patchy areas of superficial charring due to the recent surgery but most of the mucosa appeared normal. Posteriorly the wall was unusually thin, red and edematous. For several centimeters in all directions cellulitis was present in the subperitoneal fatty tissues overlying the urinary bladder. Multiple cuts were made and revealed, besides the diffuse edema of the bladder wall and areas of fibrouslike induration scattered throughout the posterior part of the bladder and involving about one third of the entire organ. No papillary processes or deep ulcerations were found. Microscopic sections of this portion of the urinary bladder revealed frequent small abscesses in a dense fibrous stroma. Large colonies of typical ray fungus were found with the pus cells in these abscesses.

The foot was approximately three times its usual size and the swelling extended up to involve to a much lesser extent the lower third of the leg. There were many tiny sinuses scattered over the skin surface. Sectioning revealed a remarkably dense fibrouslike tissue extending down to the bone. There was some destruction with softening and purulent matter in the lower end of the tibia which was continuous with the processes in the surrounding soft tissues. Smears from the purulent matter in the bone and sinus tracts revealed actinomycetes.

JOHN A. LOER, M.D.

Lich, R., Jr.: The Treatment of Inflammatory Urethral Strictures. *Am. J. Surg.* 1944 65: 38

A rapid, safe and long tried nonsurgical method of dilating urethral strictures of small caliber is outlined. The advantage of oil in the urethra as a filiform

lubricant, and the danger of oil embolism are mentioned. The necessity of frequent bladder and urethral lavage is pointed out, and the use of a 5 per cent lactic-acid solution is advised. In the noninfected case urotropin is advocated as a prophylactic, and the necessity of urinary acidity for its effectiveness is noted. Slow vertical decompression is accomplished by inserting a 20-gauge needle into the tube leading to the urine-collecting bottle. In lieu of the more complex apparatus designed specifically for gradual vertical decompression. The author mentions the possibility of urethral malignancy in instances of repeated urethral bleeding following dilatation.

The method of dilatation of urethral strictures is as follows:

1. A urethral filiform is passed through the urethral stricture.

2. A Phillips follower catheter is attached to the filiform and inserted into the bladder for drainage and dilatation. If the stricture will not permit a Phillips catheter to pass, the filiform is fixed in position for twenty-four hours, after which time a small Phillips catheter will usually traverse the stricture.

3. The bladder is decompressed slowly in the event of chronic massive retention.

4. The dilating catheter followers are increased 2 F sizes every twelve hours until a 22 F caliber is reached.

5. After a 22-F catheter follower is retained for twelve hours the follower and filiform is replaced with a 20-F soft-rubber bevel-edge catheter.

6. The rubber catheter size is increased at twelve hourly intervals until a 26-F size is reached.

7. The rubber urethral catheter is increased 2 F sizes every twelve hours until a 26-F catheter has been in position for twelve hours.

8. Further dilatation and maintenance of the accomplished urethral caliber is then continued with metal sounds used at ever-increasing intervals based on clinical progress.

ROBERT LICH, JR., M.D.

MISCELLANEOUS

Schnittker M. A., and Lenhoff C. D.: Sulfonamide-Resistant Gonorrhea Treated with Urea and Sulfonamide by Mouth. *J. Lab. Clin. Med.* 1944 31: 639.

Until recently the problem of sulfonamide-resistant gonorrhea has been an important one constituting from 10 to 20 per cent of all cases. Penicillin has now made gonorrhea, in any of its forms, curable in practically all cases.

In an attempt to find a more successful method of treatment for these cases than anterior urethral instillations of silver salts and a safer method than fever therapy, the authors were encouraged by reports of the efficacy of urea in combination with the sulfonamides as a local dressing for wounds to try urea by mouth in cases of sulfonamide-resistant gonorrheal urethritis.

Forty males whose gonorrhea failed to respond to one or more courses of sulfonamide employing 1 gm.

of sulfathiazole or sulfadiazine a day for five days were found to have smears and cultures positive for gonococci. Besides a careful history and physical examination the studies included a complete blood examination a second or third-glass urine specimen for albumin and red cells the fasting blood urea nitrogen and a twenty-four hour urine urea. When all these findings were normal the patient was started on 2 tablespoons three times a day of a mixture containing 325-gm. urea 450 cc. of distilled water and q.s. simple syrup ad. 1,000 cc. This medication was well tolerated and supplied 30 gm. of urea daily. This treatment was given alone for three days. On the morning of the fourth day another fasting blood urea nitrogen and twenty-four hour urine nitrogen were determined, a urethral smear was made and the patient was begun on a sulfonamide the same drug and in the same dosage which had failed previously. The urea and sulfonamide were given together on the fourth fifth and sixth days. The urea was then discontinued and the sulfonamide was given alone for another three days. If at the end of treatment any discharge remained smears and in some instances cultures were made. The patient's progress was followed for another three weeks by two glass tests of the urine and smears.

Of the 40 cases treated 21 (52.5 per cent) showed a rather dramatic recovery the urethral discharge ceased abruptly and completely. The two-glass test and smears remained negative and no urethral discharge reappeared during the three weeks observation period. Study of the 19 unsuccessful cases revealed no relationship of onset of discharge to time of institution of the original sulfonamide treatment. The number of previous attacks of gonorrhea was not related to the end results of urea-sulfonamide therapy nor was the number of previous courses of sulfonamide related to success or failure of urea-sulfonamide therapy.

Fifteen patients of the same type studied with urea-sulfonamides were given double the routine dose of sulfonamide treatment alone with only 3 (20 per cent) successes. In the way of further control studies, 5 patients were given the 30 gm. of urea alone for seven days with no beneficial result. Since many patients had received 1 to 2 gm. of sodium bicarbonate with each dose of sulfonamide it was necessary to perform controls on the sodium bicarbonate. Four patients had sodium bicarbonate alone and 4 patients received sodium bicarbonate in conjunction with the routine dose of sulfonamide. In neither group were there any cures.

Of the 19 failures of urea-sulfonamide therapy 8 responded to anterior urethral instillations of silver salts 2 responded to fever therapy and 9 responded to penicillin administration. Only 5 (12.5 per cent) of the 40 patients experienced any toxic effects from the sulfonamides. In 4 instances these were mild including headache drowsiness conjunctivitis and microscopic hematuria. One patient had a severe reaction with fever malaise and headache after two days of drug treatment.

Laboratory studies revealed slight increases in the blood urea nitrogen and in the twenty-four hour urine urea but drug levels of the blood remained the same. The resistant strains of gonococci were able to grow on concentrations of 0.1 mgm. per cent of sulfathiazole and 2.0 per cent urea chocolate agar plates. These strains of gonococci did not grow in the combined presence of 2.0 per cent urea and 0.35 mgm. per cent sulfathiazole.

The authors conclude that the urea sulfonamide treatment of sulfonamide-resistant gonorrhea may serve a useful purpose when penicillin is not available.

DONALD F. McDONALD M.D.

Sternberg T. H. and Turner T. B.: The Treatment of Sulfonamide-Resistant Gonorrhea with Penicillin Sodium. *J. Am. M. Ass.*, 1944, 126: 157.

Studies have been carried out in 15 selected army hospitals with a view toward determining as rapidly as possible the time-dosage factors in the treatment of sulfonamide-resistant gonorrhea with penicillin. A total of 1,686 patients refractory to at least two courses of a sulfonamide and in some cases to artificially induced fever were treated with total dosages varying from 40,000 to 160,000 Oxford units per case, the individual dose being from 10,000 to 20,000 units given intramuscularly every three hours.

These studies showed penicillin to be a remarkably effective drug in the treatment of gonorrhea. Its use usually caused a disappearance of the symptoms and a reversal of the bacteriological findings within forty-eight hours. One course of treatment with a dosage of 160,000 units per case effected cures in 98 per cent of the cases; a dosage from 80,000 to 120,000 units per case effected cures in 96 per cent and one of 50,000 units in 86 per cent. No significant differences in the final results were noted when a given total dose was administered in individual injections of either 10,000 or 20,000 units. Further more little advantage was gained by prolonging the time of treatment schedules beyond twelve hours.

Factors such as the duration of infection previous fever therapy and race appeared to have no effect on the results of therapy.

Of a total of 126 patients who failed to respond to one course of penicillin 85 were treated with an additional dosage of 100,000 units of penicillin. Of these 78 (91.8 per cent) were cured. Thus, by a second treatment of the failures cure was obtained in 99 per cent of all the cases. No case in the entire series proved to be penicillin resistant.

Complications of gonorrhea responded well to penicillin although the more serious forms of complications required prolonged treatment with higher dosage.

Reactions to penicillin were inconsequential and in no instance was it necessary to discontinue treatment for this reason.

Because of the known effects of penicillin on *treponema pallidum*, the possibility of masking or delaying the development of early syphilis must be considered.

Finally it should be recognized that the treatment of gonorrhea has been completely revolutionized in the past few years first by the introduction of the sulfonamides and, more recently by the development of penicillin. It is clear that the management of gonorrhea now belongs within the sphere of the chemotherapist and that local treatment is rarely necessary and may do more harm than good.

JOHN A. LOYD, M.D.

Page S. G., and Helms L. L.: One-Day Treatment of Sulfonamide-Resistant Acute Gonorrhea with Penicillin: A Preliminary Report. *Virginia M. Month.* 944, 71-73.

Thirty adult males all but 1 of whom had previously received one or more courses of sulfathiazole, were given intramuscular injections of a solution containing 20,000 Oxford units of crystalline penicillin in alternate buttocks every three hours until five doses (100,000 units) were given.

Fifteen of the 30 patients were bacterially negative at the end of three hours, 7 were negative at the end of 6 hours and 1 was negative at the end of nine hours. All were negative at the end of twelve hours. All of these patients were cured insofar as could be determined by an observation period of three weeks with three consecutive negative gonococcal cultures which were taken not less than one week apart and with consistently negative physical and other laboratory findings.

No toxic effects were noted; the blood counts and urinalyses done at three, twelve, twenty-four and forty-eight hour intervals were normal.

JOHN W. BRENNAN, M.D.

Riba, L. W., Schmidlapp, C. J., and Borwoeth, N. L.: The Use of Penicillin for Gonorrhea Resistant to Sulfonamide Compounds: Report of 458 Cases. *Harvard Chic.*, 944 6-73.

A series of 450 sulfonamide resistant cases of gonorrhea were treated with penicillin. One group consisted of 105 patients treated with 160,000 units, 10,000 units being given intramuscularly every three hours for forty-eight hours with 2 (2 per cent) failures. One of the 2 was cured with 1,000,000 units of penicillin. A second group consisted of 112 patients who were treated with 100,000 units, 10,000 units being given intramuscularly every hour for ten hours with 11 (9.8 per cent) failures. These 11 failures were treated again with 160,000 units with 6 additional cures. A third group consisted of 233 patients who were treated with 50,000 units, 10,000 units being given intramuscularly every three hours with 55 (23.6 per cent) failures. Forty-eight of the 55 were successfully treated with 100,000 units (1 with 160,000 unit).

The average age incidence was twenty-three years. The chief source of the infection was casual pick-ups (5.4 per cent). Ninety per cent of the patients had been previously hospitalized in station hospitals for treatment. These 450 cases of gonorrhea had all received oral sulfonamide therapy averaging about

85 gm. each without material benefit or clinical cure. The chief drugs employed were sulfadiazine and sulfathiazole.

Pretreatment examination revealed a urethra, 5 charge in 96 per cent of the 450 cases. Fifty per cent of the cases had positive smears and cultures, 12.4 per cent had positive smears and negative cultures. In 31.7 per cent of the cases in which the smear was positive no culture was made. Six patients with doubtful smears and 6 with negative smears had positive cultures. For 4 with positive smears, 3 cultures were overgrown with contaminants, and 1 with doubtful smears had a negative culture. Urethral smears were diagnostic in 95 per cent of the cases whereas cultures were of definite diagnostic value in only 3 per cent.

The chief complications of gonococcal arthritis in this series of cases were acute prostatitis (6.1 per cent), meatal stricture (13.6 per cent), urethral stricture (12.5 per cent), epididymitis (7.3 per cent), seminal vesiculitis (3.7 per cent), periurethral abscess (2.6 per cent), syphilis (2.6 per cent) and arthritis (0.6 per cent).

The average duration of infection prior to admission was forty-seven and two-tenths days. The average period required for a hospital work-up before treatment was instituted was six and four tenths days. The post treatment observation averaged twenty-three and eight tenths days. The average loss of time from the onset of infection to the return to duty was eighty-one and three tenths days per patient.

On the first clinical day following treatment 51 per cent of the patients had no urethral discharge; in 13 per cent there was only a moist meatus; but in the remainder there were from mucoid to purulent discharges. By the tenth post treatment day 76 per cent had a dry meatus, 7 per cent had a moist meatus and 13 per cent had a discharge. On the tenth day the urine was clear in 76.6 per cent of the patients. All of the prostate glands were examined during the second week and seminal fluid containing penicillin was cultured. Calibration for urethral strictures was carried out during the third week. Follow-up smears were positive in 9 per cent, doubtful in 30 per cent, and negative in 66.4 per cent of the cases. The highest incidence of positive smears was noted in the 50,000 unit group. Of cultures 3 per cent were positive and 2.2 per cent were overgrown with contaminants; the remainder were negative.

Critical review of the failures with penicillin reveals that in 61 of the 63 cases in sufficient penicillin was administered. After sufficient penicillin was given there were still 14 cases in which penicillin failed. Twelve of these 14 cases were retreated with hyperpyrexia and penicillin (100,000 units) with success in 4 cases.

Six of the 10 remaining cases were treated by intensive penicillin therapy (1,000,000 units) with 3 successes. The final 7 cases were treated with sulfapyridine by mouth, urethral irrigations and irrigations of strong protein silver solution with 4

prompt successes. One patient was found to have a contraction of the vesical neck which after trans-urethral resection was followed by cure of the infection.

The authors conclude by suggesting that a total of 160,000 units of penicillin is the desirable dose for sulfonamide resistant cases of gonorrhea and leads to cure of 98 per cent of the cases

DONALD F. McDONALD, M.D.

Culp, O. S. and Kaplan, I. W.: Condyloma Acuminata: 200 Cases Treated with Podophyllin
Ann. Surg., 1944 120 251

Podophyllin has been found to be unusually successful in producing prompt and complete disappearance of condylomata acuminata regardless of size, number, location or duration of the growths. The drug is best applied as a 25 per cent suspension in mineral oil. Anesthesia and hospitalization are not necessary. There is minimal time lost from any type of physical activity.

Most lesions disappear within four days after a single application of the drug. Growths within the urethra usually require two or more treatments. None of the authors' patients required more than four topical applications.

No ulceration or scarring results and the surrounding normal tissue usually is unaffected by the drug. In isolated cases of extensive application under long prepuces some balanoposthitis may develop but thorough washing twenty four hours after treatment will prevent this and not interfere with the end-result.

The convalescence is usually entirely painless but some patients, especially those with extensive involvement of the vagina, may require sedation during this period.

Recurrences or new growths are to be expected since the etiology of condylomata acuminata remains unknown but these likewise respond quickly and completely to the same treatment.

Podophyllin appears to be capable of destroying most types of granulomatous tissue and additional clinical applicability probably will be forthcoming.

The dramatic results obtained in this series of 200 patients with condylomata acuminata on the penis, female genitalia, perineum, scrotum, urethra and anus and the simplicity of the treatment with podophyllin recommend a more general adoption of this type of therapy.

JOHN A. LOER, M.D.

Buchwald, K. W. and Hudson, L.: The Biochemical Effects of Sex Hormones. Acid and Alkaline Phosphatase Activity, Calcium and Phosphorus. *Endocrinology* 1944 35 73.

A series of 63 mature rats were subjected to testosterone propionate and diethylstilbestrol in oil injected subcutaneously for a twenty-eight-day period. These studies were undertaken to study the biochemical process involved in the hormonal therapy of carcinoma of the prostate. The phosphorus intake and output was carefully followed. There was no change in the serum calcium or in the output of calcium and phosphorus in the feces.

The authors found that diethylstilbestrol in male rats caused a reduction of serum phosphorus and acid phosphatase activity of the serum. The alkaline serum-phosphatase activity was unchanged in contrast to the reduced alkaline phosphatase activity of the femurs. This latter finding may be a significant factor in the lack of healing in bony metastasis in patients with prostatic carcinoma.

The female rats subjected to subcutaneous injections of testosterone propionate demonstrated an increased serum alkaline-phosphatase activity which suggests that this hormone is actively stimulating to growth. In this group of animals the acid phosphatase activity of the serum and the alkaline phosphatase activity of the femurs was not influenced whereas, the alkaline phosphatase activity of the serum was increased.

The experimental data obtained is complete and tabulated for clarity. The authors readily admit that this material is in part difficult to understand but add that further work is in progress with castrated animals so that the experiments approach more nearly the picture with which we deal in the human being.

ROBERT LACY, JR., M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Lyford J., III Scott R. B., and Johnson R. W.
Jr.: Polyarticular Arthritis and Osteomyelitis Due to Granuloma Inguinale *Am J Syph.* 1944 28 583.

The authors point out that polyarticular arthritis and osteomyelitis due to granuloma inguinale are being seen with increasing frequency and having previously given the detailed findings of 1 case review 2 additional cases in this report. Bone and joint involvement is only rarely mentioned among the reported cases of granuloma inguinale but it occurred in all 3 cases reported by the authors.

A number of interesting and important facts regarding this disease are brought out in this report. In none of the patient's families was the disease found and as these patients had draining ulcers which would cause the bed covers to be soiled frequently this is strong presumptive evidence that mere contact with material from active lesions of granuloma inguinale is insufficient to spread the disease. It has been pointed out that individual susceptibility to this disease varies greatly.

It has been previously suggested by workers in this field that this disease may be a systemic one and the authors are inclined to conclude from their 3 cases that this is probably true. All of their patients had marked anemia more or less chronic, and relative resistance to therapy. The course of the disease was marked by irregular spiking temperatures over a long period of time with loss of weight of from 15 to 40 lb during the active stage of the disease and episodes of spontaneous remissions and exacerbations. The authors point out that osteomyelitis and arthritis are frequent manifestations of systemic processes and that the onset of these joint pains are at first migratory followed in a few days by a fusiform swelling of the joints of the toes and shortly thereafter by swelling and pain in the elbows, wrists, and knees. The joints become markedly swollen and ultimately develop draining granulating ulcers which rupture from within outward. None of the joints examined contained much free fluid during the acute state and the exploration of 1 elbow joint revealed the synovium to be thick and friable while the articular cartilages remained clean and smooth. Microscopic examination of a case with progressive osteomyelitis of the bones of the hand and forearm revealed granulation tissue containing plasma, cells, and macrophages filled with Donovan bodies. The authors emphasize what has previously been mentioned that the disease granuloma inguinale should be diagnosed only when Donovan bodies can be demonstrated in smears or biopsied material from the lesions. In all of their 3 cases the Donovan bodies were readily demonstrated in the specimens

prepared by the routine method of fixation and stained by the usual technique with hematoxylin and eosin.

The mode of spread of this infection was not determined in the authors' cases, but the authors are inclined to think that their cases suggest that the metastases were hematogenous rather than lymphogenous as has previously been suggested. In all of their cases there was a systemic dissemination of the disease with a massive polyarticular arthritis and, ultimately, ulceration of many of the joints and widespread destruction of the bone. The spine, the hip joints, the forearm elbow knees etc. etc. showed joint involvement, and the authors believe that granuloma inguinale can be considered a systemic as well as a local disease. No specific treatment is advocated and 2 of their patients are still under treatment while the third several years after leaving the hospital appeared to be well in good condition and with no lesions.

PART C. COLVER, M.D.

Clay R. C.: Dupuytren's Contracture: Fibroma of the Palmar Fascia. *J Surg* 1944, 120: 274

The author sets out to show that Dupuytren's contracture is due to a neoplasm, a cellular fibroma of the palmar fascia. He reviews the theory of its etiological causes. He quotes the work of Abbott, and points out that Dupuytren himself thought the disease resulted from repeated trauma. Knewel, Koch, and Mason have suggested trauma, local inflammation, lead poisoning, loss of fat with aging and embryonic malformation. Best points out that the histories of all cases are somewhat unconvincing. These authors conclude that the etiological factors in the contracture are unknown. Brooks recorded a case associated with an aneurysm of the axillary artery and Clay stated that the theory that the contracture is due to a neoplasm is not frequently proposed. Many authors are quoted, among them Ewing of whom Clay thinks that he implies a recognition of its neoplastic character.

In general all authors agree that the first symptom of contracture is a palpable nodule in the palm. The material for this study came from 22 hands of 17 patients operated upon for Dupuytren's contracture in the Johns Hopkins Hospital, Baltimore. The histological pictures of the tissues excised were surprisingly uniform. In 14 of the patients there were areas of rather cellular fibromas interspersed with areas of hyaline-appearing fascia. The fibromas were rather poorly demarcated composed of small spindle-shaped cells with elongated nuclei which contained finely granular chromatin particles. No mitoses were seen and the cells were all quite similar. While the fibromas slowly invaded the surrounding structure, they did not metastasize.

The author believes that no true conclusion is to the etiology of Dupuytren's contracture has pre-

viously been reached that a palpable nodule in the palm was the first symptom of the disease, even preceding the onset of contractures of the fingers and that there is a marked predominance of males, 15 of the 17 patients in this series being males. Among the 14 patients of this series only 1 gave any suggestive history of trauma to the palm.

PAUL C. COLOMBA, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Hurt F., and Flo B. C. Traumatic Synostosis of the Distal Third of the Radius and Ulna. *Surg* 1944, 15 804.

Whereas congenital synostosis of the proximal third of the radius and ulna is fairly common traumatic synostosis appears to be rare, only 2 instances having been reported. This article reports an instance of traumatic synostosis of the radius and ulna in a twenty seven year-old soldier who was struck across the lower forearm by a sledge hammer in 1934. Splints were applied following which he had satisfactory rotation which gradually diminished. In the last five years the arm was fixed in midpronation.

The exostosis was removed at operation through an incision on the extensor surface. A line of cleavage was found in its center which corresponded to the pseudarthrosis in the roentgenograms. Following the operation the soldier had complete painless range of motion.

The authors concluded that both the radius and ulna were traumatized without deformity to either



Fig. 2. Final results showing further absorption of the remaining stump of bridge.

which resulted in a gradually increasing ossifying hematoma, that eventually formed a pseudarthrosis

RUDOLPH S. REICH, M.D.

Mazzini O F: Interilcoabdominal Disarticulation for Hydatidosis of Pelvic Bones (Desarticulacion interilcoabdominal por hidatidosis de la pelvis osea)
Bol Acad argent cir 1944 28 371

A fifty five year-old Italian laborer had been complaining for five years of pain in the coccygeal region which radiated toward the left gluteal area. The pain was of intermittent character was aggravated by the erect position lasted a few hours or days and recurred at irregular intervals.

At the time of admission to the hospital the patient's temperature was 100.9 degrees. A tumefaction was found in the left gluteal region the local temperature was increased, and the overlying skin was red. An incision furnished abundant pus containing the staphylococcus aureus and membranes which were found to be parts of hydatid cysts. A

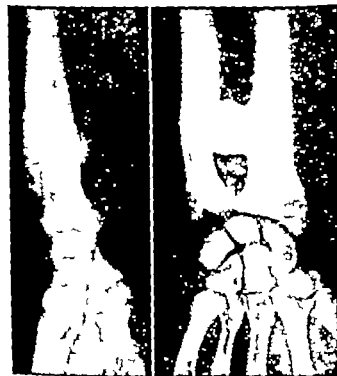


Fig. 1. Synostosis prior to surgery showing faintly a pseudarthrosis.

fistulous tract remained after the incision. Fifteen months later a fistula was still present, the secretion was seropurulent. A probe introduced 10 cm deep reached the sacrum. The sacrococcygeal region was painful to touch. The gait was slightly impaired. Casson's intradermal reaction for the echinococcus was positive. X rays revealed a sacral lesion.

A diagnosis of hydatid cyst of the sacrum was made. Under spinal anesthesia the posterior aspect of the sacrum was exposed through a Zuckerkandl incision. Fungus masses were curetted and after the sacrum was trephined, a cavity containing hydatid membranes was entered. A portion of the sacrum and coccyx was resected. A drain was placed into the wound. The after treatment consisted of injections of a polyvalent antiparasitic vaccine and the administration of sulfa drugs.

Six months later a fistula was still present. Pain had not recurred after the intervention. The fistula was treated with injections of bismuth paste.

Three years later a minute orifice surrounded by an ulcer was still present within the postoperative scar and a seropurulent secretion was noticed. Under spinal anesthesia the old scar and the fistulous tract were excised, fungus masses were curetted and a drain was inserted.

Subsequent roentgenograms demonstrated a condensation of osseous tissues.

The author concluded from his observations that the disease did not make any progress since the first intervention, but no claim of a cure could be made because minimal lesions or lesions that could not be visualized in roentgenograms may have been present. Although no biological method of therapy is efficient in 100 per cent of the cases, the employment of antihydatid vaccines is recommended after operations.

JOSEPH K. NARAT, M.D.

Christmann, F. E.: Interilioabdominal Disarticulation for Hydatidosis of the Pelvic Bones (Disarticulation Interilioabdominal pro Hydatidosis d. la pelvis ossea). *Bol. Acad. argent. ci.* 1944, 31: 386.

The author states that Leighton reported 3 cases of interilioabdominal disarticulation and collected 103 cases from the literature.

A forty-seven year-old Yugoslav peasant admitted with the diagnosis of osteochondromatosis of the right femur and hip. First experienced pains in the involved regions five years prior to admission. Gradually a hard tumor developed in the region of the anterosuperior iliac spine. The progressive growth finally caused interference with the gait. Radiotherapy had to be abandoned on account of the pains produced by it.

At the time of examination the overlying skin was only slightly altered. It had a pronounced luster and few telangiectases were visible. The local temperature was increased. The tumor had a hard consistency which, however, was not uniform.

Roentgenograms showed a distention of the superior metaphysis of the involved femur with destruc-

tion of the compact parts of the bone and invasion of the adjacent soft parts.

The slow evolution of the tumor and preservation of the general condition of the patient justified the assumption that the tumor originated in cartilaginous tissue. A biopsy furnished tumor tissue of soft consistency and white color. A diagnosis of chondrosarcoma of the femur was made. Roentgenograms of the chest did not show any metastases.

Under spinal perineal anesthesia supplemented by cyclopropane interilioabdominal disarticulation was performed. The external and hypogastric arteries were ligated. In view of the fact that the pelvis was invaded by the tumor disarticulation of the hip joint was replaced by the atypical interilioabdominal disarticulation through the pubic and sacroiliac articulations.

The patient was discharged from the hospital four and one half months after the operation. The histological diagnosis was chondrosarcoma.

In another instance an intelligent man thirty years of age was admitted with complaints of pains in the pelvic region and the inability to walk. He had difficulty in standing on his feet. Several clinics refused to treat the patient who concluded that his condition was incurable. He asked to be relieved by any means including amputation, but refused the biological treatment of hydatidosis of the pelvic bones.

The very large infected, hydatid abscess was drained and numerous sequestra were removed from the osteomyelitic coccyx. The coccyx was nearly completely destroyed and the femoral head was separated from the neck. An interilioabdominal disarticulation was performed and the patient survived the operation two years. The author performed the operation in 1911 because he was convinced that the biological treatment of hydatidosis would not exert any marked effect on the stability of the femur or the osteomyelitis of the coccyx.

The author changed his opinion since the operation was done and would now apply autogenous therapy, he would attempt to correct the dislocation by continuous traction and would treat the osteomyelitis with sulfonamides and excision of the sequestra. Calcagno's reports on the subject of biological treatment of hydatidosis sound very convincing.

In 1913 or 1914 Churo performed a successful interilioabdominal disarticulation on account of an advanced conofemoral tuberculosis. Recently Sir Martin performed a similar operation on a patient who made an uneventful recovery.

JOSEPH K. NARAT, M.D.

FRACTURES AND DISLOCATIONS

Swart, H. A., and Miyakawa, G.: Fractures of the Femur. Results of Treatment of 179 Patients. *Am. J. Surg.* 1944, 65: 221.

The authors present the results of treatment of 141 fractures in 179 patients from June 1, 1935 to May 1,

1942 All were fractures of the femur in 3 patients both femurs were broken and in 2 patients treatment was given twice for femoral fracture. There were 18 fractures of the neck of the femur 36 intertrochanteric fractures 23 subtrochanteric and upper third fractures, 69 in the middle third of the shaft and 28 in the lower third of the shaft.

Details as to age diagnosis and length of time following injury when treatment was instituted are given. Comments are made regarding each of the treatments for the different types of fractures.

The authors believe that the use of the Smith Petersen nail is still the best method of treating fractures of the neck of the femur although there have been many failures even when this apparatus is correctly applied. Certain factors militate against success in treating this fracture no matter what is done.

The Roger Anderson well-leg splint was used successfully in intertrochanteric fractures in patients who could be kept alive. The authors have had no experience with the use of Smith Petersen nails with side-arm extensions but if patients can be made ambulatory following this operation better results should be expected.

In treating subtrochanteric fractures they believe that open operation with the use of two vitalium plates is the method of choice.

Results with Russell traction in the treatment of upper and middle third fractures have been so good that they are enthusiastic about the method. Union results in a comparatively short time and the degree of knee stiffness is less than when other methods are used.

Disability following fractures of the lower third of the femur is still high, but good anatomical position of the fragments with the use of two- and three wire Kirschner traction as described has been obtained.

EMIL C. ROBINSON, M.D.

Jack, E. A.: Evacuation of the Fractured Femur; the Tobruk Plaster and Other Methods Used in the Middle East. *Lancet* Lond. 1944, 247 11.

The transportation of a casualty with a fractured femur over long distances always has been a problem of considerable difficulty. In the North African campaign a method was worked out to immobilize the leg satisfactorily—to negotiate the transportation with a minimum of pain and with the least possible chance of complication.

The surgeons in the hospital around Tobruk found the so-called Tobruk plaster very satisfactory. An extension strapping was applied to the leg, and then a long leg plaster cast was applied from the groin to the toes with gaps in the cast over both lateral regions to allow the straps to be pulled through. A Thomas splint was threaded over the plaster cast and the straps were tied around the foot-end of the Thomas splint under tension. Finally a second layer of plaster cast was used to envelop the splint and the first cast. This method had several drawbacks. It was difficult to apply a long leg plaster when the femur was shattered and the thigh completely un-

stable. The manipulation caused the condition of the already shocked patient to become worse and finally inspection of the wound during the trip was not possible. These disadvantages were partly overcome by the so-called modified Tobruk plaster.

The modified Tobruk plaster technique consisted of (1) reduction and fixation of the fracture by skin traction on a Thomas splint, and (2) stabilization of the limb and splint with plaster. The wound was surgically treated and an extension strapping was applied to the lower leg from a point about 2 inches proximal to the knee joint line. An ankle felt strap was applied. The knee was held in 15 degrees of flexion. A Thomas splint was threaded over the limb and the straps were tied around the foot-end of the Thomas splint. The leg was padded with special attention to the patella and the tibial crest.

The leg and Thomas splint were then covered with from 6 to 8 layers of loosely wound plaster-of-Paris bandages, the plaster being closely molded to the lateral side of the thigh to prevent the Thomas splint from slipping medialward. It has been found that if this was not done the Thomas ring would very frequently press against the anus and bulbous ureter and thereby cause retention. Finally a foot piece was added to prevent equinus deformity of the foot.

It is emphasized that under no circumstances should reduction of the fractured femur be attempted in this manner.

The advantages of the modified Tobruk plaster are (1) the fracture is immobilized under full view of the wound (2) the method is simple, quick and can be done at the earliest possible opportunity, which reduces operative shock and (3) the thin layer of cast can be easily removed and very easily replaced if it should become necessary to inspect a wound.

GEORGE I. REISS, M.D.

Truog, C. P. "Ring Sequester as a Complication of Fixed Skeletal Traction." *Am. J. Roent.* 1944, 52 64.

Steinmann pins were passed through the upper tibial fragment and the lower tibial fragment or calcaneus in 6 male patients of various ages (2 negroes and 4 whites) all suffering from fracture of the tibia and fibula. The pins were incorporated in plaster casts which extended from the toes to above the knees with about 15 degrees of flexion at that joint. The patients then became ambulatory.

All of these patients complained of pain about the upper Steinmann pin and all developed draining sinuses following removal of the pins in from ten to forty-eight days after they had been inserted. Roentgenology disclosed in each case, in addition to more or less delayed union, a typical "ring" sequestrum consisting of abnormally dense shadow around the canal from which the pin had been removed and a fairly marked resorption of bone around the ring of dead bone itself. Sequestrectomy confirmed the diagnosis in 5 instances.

A seventh report is appended in this case Kirschner wires were used the consequent sequester not

being as clearly demonstrated as the sequestra occurring with the use of the Steinmann pins.

The etiology of these sequestra is probably pressure necrosis plus a low grade of infection.

JOHN W. BROWNMAN, M.D.

ORTHOPEDICS IN GENERAL

Rosenberg, E. F., Baggenstoss, A. H. and Hench, P. S.: The Causes of Death in 30 Cases of Rheumatoid Arthritis. *Ann Int. M.* 1944 30 903

Of 30 patients of rheumatoid arthritis at the Mayo Clinic who underwent autopsy examination after death, 10 died from the rheumatoid arthritis itself, 8 died because of the treatment itself and 12 died of causes which were unrelated to the arthritis or the treatment.

Cardiac lesions were found in 24 cases to which death was directly attributable in 7 patients. In 3 instances, death was preceded by congestive heart failure with anasarca. One death was the result of coronary occlusion, myocardial degeneration, and edema in a child aged nine years. Four patients died from active subacute or chronic rheumatic carditis without pulmonary or systemic edema, the heart failure resulting from active rheumatic inflammation in every case.

There were 2 deaths due to the kidney condition the result of acute pyelonephritis and oliguria following typhoid fever therapy.

Chronic bronchiectasis and diffuse pulmonary supuration were responsible for 2 deaths and in 3 instances death was the result of massive pulmonary embolism 2 of the latter deaths occurred after orthopedic manipulations and the application of casts. Three patients died from bronchopneumonia which was acquired during the course of treatment of the arthritis. Two deaths were caused by pulmonary fat embolism which may have been the result of fat released following manipulation or the result of fractures of osteoporotic bone containing large marrow spaces filled with fat. There was 1 instance of death resulting from massive collapse of the lungs in a male aged thirty-four who was overweight and had severe spondylitis and a large incisional hernia.

Two patients died after long periods of chronic diarrhea, the result of exhaustion.

It is suggestive from this study that rheumatoid arthritis is associated with or predisposes patients to certain fatal visceral lesions, the most striking being rheumatic heart disease. There was a high incidence of cardiac lesions similar to those of rheumatic fever although there was a history of rheumatic fever in only 2 of the 30 patients.

It is noteworthy that the deaths related to therapy were unusually high. Ordinarily harmless medical and orthopedic procedures proved fatal.

Although renal lesions are rare in rheumatoid arthritis and common in gouty arthritis microscopic renal lesions were frequently encountered.

RUDOLPH S. REICH, M.D.

Dandy, W. E.: The Treatment of Recurring Attacks of Low Backache Without Sciatica. *J. Am. M. Ass.*, 1944, 135 75

Defective discs are caused by an inherent weakness of the lumbar spine due to a shift of the planes of the lateral articulations between the last three lumbar vertebrae and the sacrum. Normally in the first two lumbar vertebrae the lateral joints parallel the spinous processes. In the third lumbar vertebra the plane of the lateral joints is turned laterally from 15 to 25 degrees. In the fourth from 25 to 45 degrees, and the plane of the lumbosacral joint forms a 60 degree angle with the spinous processes. Trauma causes these joints to loosen and transfers increasing injury to the discs.

The gross pathological changes in the so-called concealed discs are characterized by a small protrusion, fluctuation, adherence to surrounding structures, and by opacity of the overlying ligaments. When incision is made the instrument dips into a cavity and frequently sequestra can be extracted.

The mechanism of pain and sciatica in defective intervertebral discs cannot be stated with certainty. It is believed that swelling of the joint capsule or slipping of the lateral facets is responsible for unilateral backache. However, a combination of all three, lateral joints and disc, is in one way or another responsible for the backache.

The history usually reveals recurrent attacks of low back pain with or without sciatica. The attack usually lasts from two to three weeks and is brought about by a heavy lift, sudden twist, or sudden movement or there may be no apparent precipitating cause.

It is possible to make a diagnosis of defective disc causing backache from signs and symptoms and x-ray findings in from 95 to 98 per cent of the cases. Recurring attacks of low lumbar backache associated with sciatica are pathognomonic subjective evidence, and narrowing of an intervertebral disc observed by means of x rays is objective evidence of defective discs.

The inadvisability of the use of contrast medium for the diagnosis of defective discs is illustrated in the following four points:

1. Only large discs produce a filling defect; these comprise only 25 per cent of the cases.
2. The information gained is unreliable.
3. Their use is painful.
4. There are temporary or permanent after effects.

Spinal tumors, especially tumors of the cauda equina, present the only difficulty in the differential diagnosis. If tumors are suspected a lumbar puncture is indicated. When a disc is defective the vertebral body is more movable than normal. When the spinous process is pushed caudally with an instrument, increased mobility can be elicited, and this is indicative of a defective intervertebral disc.

The operative treatment has for its objective the complete removal of the disc by curettage and the baring of the bone surfaces to allow bony union.

occur. The bone surfaces offer a broad surface for fusion. Stabilization of the lateral joints usually follows. Fusion of the lateral joints has no practical value because of the minor part they play in the stabilization of the spine. It has been shown that there was no movement in the joints three months after removal of the disc.

Spinal fusion is never necessary in the treatment of ruptured intervertebral discs. It has been used by neurosurgeons who had obtained poor results following removal of the disc alone. There are two reasons for the unsatisfactory results:

- 1 Failure to remove the disc completely
- 2 Failure to recognize multiple intervertebral discs

A total of 32 discs were removed from 20 patients. Approximately 25 per cent were of the large variety. The remainder were concealed discs. The author found multiple discs in 80 per cent of the cases.

There are three possible causes for continuing pain after operation:

- 1 Recurrence of the original disc, which is very unlikely
- 2 Another disc that was missed
- 3 A tumor of the spinal cord or cauda equina (1 per cent)

Psychoneurotic backaches are nearly always continuous, are not accentuated by coughing or sneezing and have a tendency to spread to the shoulders and head. Such extensions have no organic basis.

GEORGE I. RUSS, M.D.

Swartout, H. O., and Frank, W. P.: Multiple Familial Cases of Poliomyelitis. *J Am M Ass* 1944, 125: 488.

Of a total of 721 patients with poliomyelitis admitted to the Contagious Disease Unit of Los Angeles County Hospital in 1943 the author found that 67 cases or 9.29 per cent, came from families with multiple cases. This is compared to the figures of the previous five-year period (1938 through 1942) in which of 403 cases of poliomyelitis reported to the Los Angeles County Health Department only 22 cases or 5.4 per cent were in families with multiple cases.

This difference between 9.2 and 5.4 per cent in the incidence of multiple familial cases is attributed to the fact that in 1943 not only were cases diagnosed by the finding of flaccid paralysis and the other acknowledged signs of poliomyelitis but, in addition the presence of muscle spasm was taken into account. The author stresses the presence of muscle spasm in the diagnosis of poliomyelitis. Though mild degrees are often difficult to perceive and may be missed the type of spasm characteristic of poliomyelitis may continue for weeks or months thus being differentiated from the temporary muscle soreness and stiffness which accompanies other diseases.

To confirm the diagnosis spinal fluid examination was done in 66 of the 67 cases. Two cases showed bloody taps but of the remaining 64, 52 or 81.2 per cent had spinal-fluid findings of more than 10 cells per cubic centimeter or a total protein above 65 mgm per cent and thus were considered positive. The author admits that in the cases unconfirmed by spinal-fluid examination and without physical findings other than persistent muscle spasm the diagnosis of poliomyelitis cannot be definitely established. Nevertheless the diagnosis appeared justifiable when the history was suggestive and when muscle spasm persisted for weeks after the temperature became normal.

The 67 cases diagnosed in 1943 were also reviewed in the light of diagnostic criteria used in previous years. Studied in this way it was found that of the 67 cases, 12 would not have been recognized and 5 probably would not have been recognized.

It is the author's opinion that the concept of spasm in poliomyelitis makes it possible to diagnose cases on the basis of very mild physical findings. Also the lack of recognition of these cases in previous years may account somewhat for the difference between the large number of adults who have protective substances in their blood against the poliomyelitis virus and the small number who have had the disease. One-sided spasm unrecognized and untreated may also account for the frequent orthopedic problems of unexplained scoliosis and leg shortening.

DANIEL H. LEVINTHAL, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Northcroft, G. B. and Morgan, A. D.: A Fatal Case of Traumatic Thrombosis of the Internal Carotid Artery. *Brit J Surg* 1944, 35

A signalman aged thirty-one was walking along a military road, when a piece of loose rope dangling from a lorry travelling in the same direction wound itself around the patient's neck, threw him to the ground and then unwound itself without dragging him along. Though he felt faint and was suffering from a superficial laceration in the right parietal region the patient was able to walk to the Unit Medical Officer. At the nearest reception station a single stitch was inserted in the scalp wound. Bruising of the left side of the neck was noted and the patient suffered slight amnesia. On the following morning his neck showed superficial abrasions more marked on the left side with a swelling of the left sternomastoid muscle just above the clavicle which was thought to be a hematoma. Superficial examination of the central nervous system showed no abnormality. An hour later while the scalp wound was being redressed, the patient did not respond readily when spoken to; twenty minutes later he had lapsed over in bed and jerky movements occurred in the right arm and leg. Fifteen minutes later he was completely unconscious could not be roused, and had a complete right flaccid hemiplegia. Two hours later an exploratory temporal burr hole was made. There was no evidence of extradural bleeding, the dura was not tense and on incision, normal cerebrospinal fluid escaped. The left lateral ventricle was tapped and 5 cc. of clear colorless fluid were withdrawn and the wound was closed. Seven hours later his unconsciousness had increased to deep coma, the temperature was normal, pulse 40 and irregular, and respiration so. The right hemiplegia remained unchanged and he had developed cataplexia in the left arm. On the following morning forty-eight hours after the accident and nineteen hours after operation, his general condition became worse and he died.

At postmortem examination two-thirds of the left sternomastoid muscle was found to have been ruptured a thinned-out strip of muscle being left at the level of the injury. The first 1½ inches of the left internal carotid artery were transformed into a hard bluish spindle-shaped swelling as a result of traumatic thrombosis. The main thrombus lay just above the origin of the internal carotid artery extending upward for 1½ inches. The original lesion was presumably a tearing of the intima and media with extravasation of blood into the media which raised both the intima and media from the outer layers of the vessel wall. As the hemorrhage increased in size, the lumen of the vessel became narrowed and finally it was completely obstructed in the

form of an inverted valve with the thrombus blood below it. Following total occlusion, more recent thrombosis occurred above the level of the injury spreading upward into the petrous and cavernous portions of the vessel to continue into the left middle cerebral artery which resulted in massive infarction of the left cerebral hemisphere. The spread of thrombosis was found to involve the left half of the circle of Willis and most of the left middle cerebral artery.

HAROLD C. OGDEN, M.D.

Tubbs, O. S.: The Effect of Ligation on Infection of the Patent Ductus Arteriosus. *Brit J Surg* 1944, 3

Nine patients from fifteen to twenty-six years of age were operated upon for patent ductus arteriosus complicated by subacute endocardial infection. Essentially the technique used was that originated and described in detail by Gross (*Ann. Surg.* 1939, 110:321). Six of these patients are well to-day from fifteen months to over four years after operation. The type of bacterial infection (streptococcus viridans haemophilus influenzae staphylococcus streptococcus viridans and Gram-negative bacilli) which complicated the anatomical anomaly did not seem to exert any effect on the operative result. Although the bacteria in the blood might persist for some time following the ligation, the blood would eventually become sterile, the diastolic pressure rise permanently to normal figures, the murmurs practically disappear or markedly regress, the patient's physical powers rise, and the body weight and development proceed more satisfactorily than before the operation. This dramatic turn in events occurred in 1 patient in whom the sulfonamides had previously failed to curb the septic manifestations.

Of the 3 patients with fatal results one lived for eight weeks and died of complications not strictly ascribable to the operation itself, another succumbed to acute heart failure at the time of operation, and the third died following an incorrect diagnosis, there being two aneurysms of the pulmonary arteries which in a preoperative roentgenogram were overlooked or falsely interpreted as an enlarged gland. This patient lived for four months after operation and apparently died as a result of recently developed concurrent involvement of the mitral and aortic valves. The pulmonary end of the opening into the operatively obliterated ductus arteriosus was free of granulations but unfortunately there was no evidence to determine whether granulations had been present originally.

As a result of the author's experiences with this condition he concludes that symptoms of infection complicating a patent ductus arteriosus must now be considered an absolute and urgent indication for operation, that the supervention of infection should be diagnosed early and that any patient with a

patent ductus who runs an unexplained fever for more than two weeks should be suspected of this complication
JOHN W. BRENNAN, M.D.

BLOOD TRANSFUSION

Shies, E. L., and Lederer, M.: Uncontrollable Hemorrhage after Dicumarol Therapy with Autopsy Findings. *Ann Int M* 1944, 31: 332

A case is presented in which an uncontrollable dicumarol state was produced and in which the bleeding that ensued was a contributory cause of death. The patient, seventy-nine years of age, was admitted with bleeding of the gums of five days' duration and hematuria of three days' duration. She had received 500 mgm. of dicumarol orally each day for twenty-one days because of a diagnosis of thrombosis of a retinal vein, and during this period no prothrombin estimations had been made. Citrated transfusions were partially but ineffectually successful in combating the dicumarol state.

The authors warn that this drug should not be given unless daily blood prothrombin and coagulation times can be accurately determined and the patient is kept under close observation.

WALTER H. NADLER, M.D.

Malzels, M.: Processing of Plasma with Kaolin. *Lancet Lond.* 1944, 247: 205

Blood banks particularly in wartime carry reserves in excess of probable needs and to avoid waste plasma from surplus blood is retained for use in shock. The present article describes the processing of such plasma with kaolin and suggests that the resulting product when employed therapeutically is less likely to produce toxic reactions than material that is not treated with kaolin.

Normal plasma and serum are more or less opaque and the development of opalescence due to the growth of contaminating bacteria will be masked by the cloudiness originally present. Hence in order to eliminate infection as far as possible and to obtain a clear fluid in which the growth of any surviving bacteria may be quickly detected it has been customary to filter the plasma before it is stored. Unfortunately filtration does not completely solve the storage problem for both filtered and unfiltered plasma and serum contain unstable substances. In the case of plasma, these are fibrinogen and a lipoid-globulin complex while in the case of serum the complex alone is the chief cause of instability. The instability of plasma is actually enhanced by passage through filter pads which convert fibrinogen into fibrin. This fibrin then appears as clot in any filtrate obtained and eventually clogs the filter pads and brings filtration to an end. There are several methods of removing fibrinogen from plasma, but most of these fail to deal with the residual lipoid-globulin complex. This complex is finely dispersed in fresh plasma and serum but aggregates and precipitates during storage and thus reproduces the original problem of a murky fluid in which cloud

may be due either to bacterial infection or to sterile organic deposits. McFarlane's ether freeze process (1941) removes both fibrinogen and lipoid-globulin complex and gives a clear sparkling stable fluid but for technical reasons it is unlikely to come into general use until after the war. Other methods of storing liquid plasma are more or less makeshift. Removal of fibrinogen and filtration are common to all and under favorable circumstances the liquid product may remain clear for about a year.

Because of the difficulty of keeping liquid plasma and serum the present tendency is to avoid storage of liquid products and to dry all material after spin-freezing, it being assumed that if the liquid material were apparently sterile before drying then no infection of the dried product would occur in its sterile container. It follows that to ensure sterility before drying the liquid to be processed must first be filtered and this in the case of plasma necessitates a preliminary removal of fibrinogen. In general therefore the processing of plasma involves filtration and this in turn demands defibrination.

The author describes his method of removing fibrinogen from plasma by adsorption on kaolin. This method adds nothing soluble to the treated plasma and may perhaps remove toxic substances. After removing the fibrinogen the product obtained may be filtered and dried.

Transfusion with this material has been particularly free from reactions. J. M. MORA, M.D.

Lyons, R. H., Jacobson, S. D., and Avery, N. L.: Increases in the Plasma Volume Following the Administration of Sodium Salts. *Am J M Sc* 1944, 208: 245

It has been demonstrated that the plasma volume does not remain fixed even with mild dehydration and will decrease in proportion to the severity of the dehydration. In normal subjects dehydration induced by the administration of a low salt diet and ammonium chloride or by the intravenous administration of 2 cc. of mercupurine is associated with a significant fall in the plasma volume. Under these circumstances it appears that the plasma volume is not well supported by the extracellular fluid and that the loss of water and salt, coincident with the diuresis, is associated with the fall in plasma volume.

The authors note that if the plasma volume is reduced by relatively small decreases in the body water it would appear likely that the reverse situation would also be true. The administration of sodium salts sufficient to produce a positive sodium balance along with sufficient water should increase the volume of the extracellular fluid and presumably the plasma volume as well. These studies were undertaken to evaluate the effect of ingestion of large amounts of sodium salts with water *ad lib* on the plasma volume of normal subjects. The methods employed are given in detail.

From results obtained by the authors it is apparent that the addition to the diet of large amounts of sodium bicarbonate or sodium chloride results in sig-

nificant increases in the plasma volume. The consistent increase in weight noted in these subjects was the result of the retention of sodium and water and represents chiefly an increase in the extracellular fluid portion of the total body water. Although there was considerable variation between the change in the plasma volume and the change in the body weight after the first day of sodium-bicarbonate administration a fairly constant relationship was shown between the change in the plasma volume and the change in body weight at the end of forty-eight hours. The authors note that the plasma volume of normal subjects cannot be assumed to be constant as it will vary with reasonably small changes in the water content of the body and presumably with the sodium balance of the individual.

The increase in the plasma volume following the administration of sodium salts with fluids *ad lib* suggests that this might be useful in the restoration of the plasma volume after bleeding in individuals who may be mildly dehydrated. These studies suggest that the administration of large amounts of sodium salts as a preoperative measure will increase the plasma volume as well as predispose to a favorable water balance. This might be of value when a considerable blood loss is anticipated.

The hematocrit, hemoglobin concentration, and red blood-cell count fail to change in proportion to the change in the plasma volume. The cell elements in the antecubital vein from which the samples were drawn had not undergone the degree of dilution found by the direct determination of the plasma volume. Ebert and Stead explained that there are shifts in the concentration of red blood cells between the smaller and the larger vessels with alterations in the plasma volume, and that the cell plasma ratio for minute vessels is lower than for large arteries, veins, or bleeding capillaries.

The serum-protein concentration fails to change in proportion to the alteration in the plasma volume. Madden and Whipple explain that the serum proteins are in a state of dynamic equilibrium and may easily enter or leave the blood stream according to the stimulus so that the concentration remains relatively stable.

The increase in the venous pressure in these cases may be explained either as a result of an increase in the local venous pressure due to an increase in the tissue pressure or as a result of an increase in the auricular pressure. The variability in the rise in venous pressure noted in these cases suggests that in some instances the factor of local obstruction may play an important role. In any event, the increase in the venous pressure noted in the antecubital vein would be associated with some increase in capillary stasis either local or generalized which would promote greater transudation of fluid from the capillaries into the interstitial tissues.

The considerable variation between the increase in plasma volume and increase in body weight noted after the first twenty-four hours on sodium bicarbonate compared to the more constant relationship in

forty-eight hours suggests that the equilibrium between the plasma volume and extracellular fluid disturbed by the addition of salt and water had not been re-established in twenty-four hours. The gain in plasma volume may be at first quickly lost to the extracellular fluid spaces. With increases in the amount of fluid in the interstitial spaces the tissue pressure will be increased and will result in a decrease in the amount of fluid leaving the capillaries. At the same time, protein is added to the blood so that the osmotic pressure in the capillaries does not significantly fall as a result of hemodilution, and the plasma volume may thus be maintained. If such a hypothesis be true it should be expected that considerable variations would be found in normal subjects according to the rate of absorption of water and salt, the rate of excretion, the volume of extracellular fluid, the tissue pressure, the capillary pressure, and the serum-protein concentration.

HENRY F. TURNER, M.D.

Turner O. E.: Investigation of Transfusion Reactions. *Pennsylvania M J* 944, 47, 1071.

Transfusion reactions are still prone to occur despite careful methods of establishing blood compatibility. In view of the complex array of blood constituents it is surprising that potential or actual reactions are not of more frequent occurrence.

In speaking of compatibility and blood groups, it must be assumed that the plasma contains two agglutinins (a and b) and that the erythrocytes contain two corresponding agglutinogens (A and B). The blood type depends on the agglutinin.

Some have been misled in thinking that as long as the donor and recipient are of the same blood grouping (O A B AB) a compatibility exists which is sufficient to avoid reactions from the transfusion of whole blood. Such a generality is not the case and more specific methods of determining compatibility must be employed.

The specific compatibility requirements of whole blood are:

1. Similar blood grouping of recipient and donor. The idea of the "universal donor" and the "universal recipient" is now obsolete but is occasionally used in unusual emergencies. It is now recognized that there are atypical agglutinins with subgroups of A and AB.

2. Careful cross-matching of donor and recipient. The donor's erythrocytes must be compatible with the recipient's serum, and the donor's serum with the recipient's erythrocytes.

3. The donor and recipient should be checked for Rh compatibility in routine transfusions. This can be done very simply by performing the Rh typing at the same time as the blood grouping.

4. Special tests should be made to rule out atypical cold and "warm" agglutinins.

The specific compatibility requirements of plasma are:

1. Pooled plasma, which is a careful combination of all types of plasma (O A B AB) mixed into

quantities of 2,000 cc. or larger, and preferably stored for thirty days under refrigeration. This material can be maintained in the liquid state for six months in the frozen state for three years and in the desiccated state indefinitely.

2. Type-specific plasma may be prepared but is usually not practical.

In any consideration of blood compatibility it is necessary to mention the practical application of the Rh factor. Investigations have recently shown that the Rh factor may produce hemolytic transfusion reactions, and that it has a relation to the cause of erythroblastosis in newborn infants.

It has been shown that 91 per cent of mothers of infants affected with erythroblastosis were Rh negative in contrast to the usual 14 per cent in the general population. Also the majority of the affected infants and their fathers were Rh positive. It is theorized that the Rh positive fetus stimulates the production of Rh agglutinins in the mother's blood, and that these isogglutinins from the maternal circulation traverse the placenta into the fetal circulation. In the fetus the anti-Rh or isogglutinins produce either hemolysis or suppression of the erythroblast maturation thus the name erythroblastosis foetalis.

The Rh factor therefore is of special clinical importance when blood transfusions are indicated for women and infants. Women who give a history of previous miscarriages and women who have borne children with erythroblastosis should always have a compatible Rh group-specific blood transfusion. In infants with erythroblastosis (baby usually Rh positive) a transfusion of Rh-positive, group-specific (or Group O) blood should be administered.

Transfusion reactions at the author's hospital have been investigated as to probable cause and a practical system of classification has been evolved.

Comparison of whole blood to plasma transfusion reactions for 1943 showed a per cent ratio of 7.5 per cent for whole blood to 1.2 per cent for whole plasma transfusions.

In the investigation of each blood transfusion reaction the final diagnosis of the recipient was obtained. In most cases the diagnosis was supported by clinical and laboratory data.

The following is a summary of the findings.

Thirty-seven per cent of the recipients had a diagnosis of malignant disease (carcinoma 27 per cent, miscellaneous 10 per cent).

Twenty per cent of the recipients had a diagnosis of thrombocytopenic purpura, bleeding peptic ulcer or pneumonia.

Forty-three per cent of the recipients had miscellaneous diagnoses.

In spite of the fact that donors were carefully selected and compatibility techniques were carefully watched, there remains the fact that a certain percentage of patients with a diagnosis of malignancy were prone to develop a blood transfusion reaction.

If blood transfusions are to continue in scientific popularity and to compete with the safety of pooled

plasma in transfusions improved methods of determining blood compatibility must be forthcoming.

STEPHEN A. ZEMAN, M.D.

Bradley W. H., Louth, J. P. and Maunsell, K.: Homologous-Serum Jaundice. *Bull. N. J.*, 1944, 2: 268.

The occurrence of jaundice in man after the administration of human blood products (plasma and serum) is now a well recognized phenomenon. This homologous-serum jaundice which is of hepatic origin is readily distinguished from the hemolytic icterus which may arise immediately after transfusion with incompatible blood or out-of-date stored blood. Clinically it is similar to, if not indistinguishable from epidemic hepatitis (catarrhal jaundice) but the incubation period is unusually long—commonly from two to three months in contradistinction to the twenty to forty-day period believed to occur in epidemic hepatitis.

A high incidence (57 per cent) of this jaundice has been observed by the authors among 71 subjects during the course of an investigation into allergic reactions to human serum. All of these subjects received pooled human serum from a single batch a few of them received in addition whole blood or serum from other batches. This batch was however the only common factor and was clearly incriminated as being icterogenic. Subsequently icterogenicity was confirmed by the results of the deliberate administration of this batch to 4 volunteer patients with rheumatoid arthritis in whom it was desired to produce jaundice for therapeutic reasons.

The dose of homologous serum administered varied from 0.1 to 1,200 cc. The attack rate was of the same order whether the serum had been given intradermally or intravenously and whether it had been given as a single dose or in repeated doses. The severity of hepatitis which in all cases was mild or moderate in degree only also appeared to be unrelated to the size the route or the frequency of injection. There was a suggestion however that the latent period was shorter when the material was given in the larger or in repeated doses. There is no evidence, so far, that permanent liver damage ensued. The incidence of jaundice was no greater in the allergic subjects than in the normal controls.

When the syndrome occurs after inoculation of measles convalescent serum or yellow fever vaccine it is relatively easy to detect icterogenic batches of material because in most instances serum from only a single batch has been given. When jaundice follows transfusion it may be impossible to decide which is the causative batch, because in the usual transfusion practice several batches of plasma or serum may be administered to a single patient and not infrequently whole blood is given as well.

In the authors series the clinical features and the biochemical findings were indistinguishable from those of epidemic hepatitis.

Ictericogenic batches of human serum and plasma cannot be detected by any laboratory or animal

tests. Their recognition is possible only when accurate records of the batch and bottle numbers of blood products given to patients are kept, and when a careful follow up of all recipients is practiced for some months afterward. JOSEPH K. NARAT, M.D.

Maunsell K.: Desensitization in Allergic Recipients after Serum Transfusions. *Brit. M. J.* 1944, 2 36

In the attempt to determine whether an allergic state in the recipient might not be an etiological factor in the development of allergic transfusion reaction, 53 patients whose ages ranged from eleven to forty three years, who gave positive skin reactions to one or more of the tested atopens (pollen dust, milk egg) and in whom reagins (Coca's atopy) were transferable to normal individuals (Coca's atopy) were tested with reconstituted dried pooled human serum and with auto- and iso-sera with intracutaneous injection and finally with repeated transfusions of the first cited serum.

In the intracutaneous tests all the high-grade positive reactions, and a great preponderance (77 per cent) of all the positive reactions were obtained in this group with the pooled serum (For details on the control groups please consult original article.) With the unpooled fresh sera it was found that the sera did not cause any more reactions when procured from atopic donors than when obtained from non-atopic individuals, but that as before reactors were in the main atopic recipients. No positive results were procured with iso-sera even among the atopics, and no influence on the results of the different blood groups was discoverable.

Among those given the test of transfusion, 17 were atopics and only 14 of these atopic individuals gave reactions. These reactions usually consisted of erythema from splotches to large confluent patches, raised wheals running together at times to form large white edematous zones these were preceded and accompanied by itching, running nose, streaming of the eyes, and tightness of the chest. Finally in a few cases there was a state of collapse (falling blood pressure and rapid pulse). In all attacks considered sufficiently grave adrenalin was given and it controlled the symptoms satisfactorily. Even the most severe attacks were over at the end of two hours. Rigor and rise of temperature occurred independently of the rashes.

Eleven of the 14 patients who reacted were retransfused two weeks later from the same serum pool and 10 showed definite signs of desensitization. Finally 7 of those who had developed an urticaria with the first transfusion were given a third transfusion again two weeks later and of these 5 did not react at all and 2 showed some erythematous areas, but not wheals. One boy eleven years of age, again developed a rash.

Maunsell concludes that the cause of the transfusion reaction lies in the recipient rather than in the donor in allergic cases, and that repeated transfusions result in a desensitization rather than a sensitization, of the recipient. However, in some cases, follow-up observations on these recipients revealed homologous serum jaundice, which discourages further attempts at desensitization of allergic patients with human serum at present in this country.

JOHN W. BUCKLEY, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Lowdon A G R : War Wounds of the Abdomen
Report of 64 Cases Treated by Laparotomy
Edinburgh M J 1944, 51 257

The author reports 64 cases all treated in a field surgical unit with the Eighth Army between El Alamein and Tunis and 19 cases treated during the Sicilian campaign. These cases are the only ones among a total of 744 battle casualties treated by operation on which he performed laparotomy and full records of the injuries and operations are given.

An operative mortality of 45.8 per cent among the whole series and more particularly of 44.0 per cent among the 25 patients with lesions of the colon appears to represent significant improvements over the results reported for the last war.

The methods of treatment are discussed and the improvement obtained is ascribed to the following measures:

- 1 Early and adequate resuscitation with intravenous infusions of blood and plasma.
- 2 The practice of exteriorization of damaged colon whenever practicable.
- 3 The intraperitoneal administration of sulfa diazine.
- 4 Immediate postoperative establishment of continuous gastric suction in all cases with peritonitis or intestinal lesions accompanied by adequate intravenous infusions of glucose-saline solutions.

HARRY W FINE, M D

Ross, K. C. and Ryan W P : Gas Gangrene at an Australian General Hospital in the Owen Stanley and Buna Gona Campaign *M J Austral* 1944, 2 35

From November 1 1942 to February 28 1943 there were 1,815 Australian battle casualties admitted to and treated at a general hospital. There were 82 patients with clinical gas gangrene and of this number 12 died. The patients arrived at the hospital from twelve hours to six weeks after being wounded. In 70 of the cases gangrene was obvious when the patient arrived at the hospital. The 3 other cases were believed to be examples of latent infection and they are described in detail.

In the first case a minor wound was excised in the hospital two days after the wound was received. Two days after operation a fulminating edematous gas infection developed and death ensued. In the second case the wound was partially excised in the field. Here some foreign material was removed through a new incision. The original wound looked clean but two days after the second operation a fulminating edema occurred and the patient died. In the third case a foreign body was removed from the wound and three days later this patient died from a fulminating edema.

A table showing the distribution of the wounds and the number of amputations and deaths is included. By far in most of the cases gas gangrene was confined to wounds in the buttock thigh leg and foot and shoulder and arm the forearm and hand amputation stumps and the trunk showed considerably less. In some of the cases there were multiple anatomical parts involved.

The diagnosis was made from the typical stench the appearance of the tissues the presence of gas in the wound the demonstration of gas in the tissues the presence of anaerobic clostridia in wound culture, and by means of x rays.

The diagnostic points suggested as being quite important are discomfort and peevishness after operation rapidity and threadiness of the pulse intense and rapidly recurring anemia and icterus.

Clinically the cases showed a wide range, from a local abscess to widespread fulminating edema. In 3 patients there was little evidence of infection in the wound itself but an acute overwhelming cellulitis spreading from the wound commenced four or five days after the wound was received.

The bacteriological findings showed an anaerobic clostridia in 48 of the 51 cases cultured. The clostridium welchii was present in 30 cases.

All patients with gas gangrene were given a full course of 35 gm. of sulfanilamide 6 gm per day were administered until the course was completed. Sulfanilamide powder also was dusted into the wound. Gas-gangrene antitoxin was administered to 51 patients in dosages of from 20,000 to 200,000 units. Forty patients received transfusions of blood and plasma (1 liter of blood and 1 liter of plasma).

The authors soon learned to rely more and more on radical excision no matter how old the wound was. Drainage is of paramount importance and it must be remembered that fluid runs downhill. At the completion of the operation the wound was cleansed with hydrogen peroxide and saline solution and dusted with powdered sulfanilamide. Then it was filled with vaseline and covered with vaseline gauze. The extremity was then enclosed in soft dressings or plaster. X ray therapy was given in adequate doses to 1 patient only this patient proceeded to a fatal termination.

RICHARD J BENNETT JR. M D

Blood Transfusion during the Battle of Maroth
with Special Reference to Problems of Supply
J R Army M Corps 1944 83 7

This article discusses the problem of supply maintenance and distribution of blood transfusion stores under battle conditions beginning with the El Alamein campaign. The plan originated with a Base Transfusion Unit which was responsible for all supplies of apparatus and fluids. It, moreover, was responsible for preparing and supplying intravenous and intraperitoneal sulfonamides.

During battle excluding whole blood the quantity of stores required by a corps area approximated $\frac{1}{4}$ tons a day. One hundred twenty bottles of blood per corps per day was required at the beginning of a battle. A separate unit maintained the supply between the base and the forward area and the main supply section was located at an Advanced Air Transport Center.

During periods of calm, the Forward Supply Unit kept its refrigerator half full of blood. Seven days before battle 100 bottles a day were flown in until it was fully stocked which usually meant over 800 pints. In addition stocks of plasma serum and saline and sulfonamide preparations were augmented. The Advance Blood Bank was situated 5 miles behind the front line whereas the Main Supply Section was about 30 miles behind.

As soon as serious resistance was encountered one Field Ambulance opened out as a Surgical Center and a landing strip was prepared close to it for the evacuation of casualties by air. Transfusion stores were carried back and forth from the Main Supply Section by ambulance planes.

STEPHEN A. ZIEGLER, M.D.

Code S: War Surgery in the Royal Air Force. *Brit J Surg* 1944, 3

Excluding major catastrophes, such as collisions in midair, power dives to earth or into the sea, and the burning of the plane in air where death is instantaneous or occurs within a few hours, and exclusive of fractures (mentioned only in connection with discussions of organization of the services) the conditions arising in connection with the operations of the R.A.F. which require surgical aid are burns, wounds, frost-bite, immersion injuries, and head injuries.

The burns typically coming to treatment in the R.A.F. are relatively small in extent, localized to the hands and face, and of second or third degree. They are largely left alone at first, but provision is made for warmth (wrapping up), oxygen, morphia, plasma and vaseline or antburn jelly (3 per cent sulfonamide in a water-soluble base). For hand burns the Stannard glove, containing weighed amounts of one of the sulfonamides, may be applied at once. Later there is instituted either the closed method with tannic acid or other coagulant, or in burns of the face, hands, genitals and perineum, the "open method" with vaseline-gauze, tulle grass, saline packs, and C.T.A.B. in lanette wax, and with local application of sulfonamides. Early skin grafting and the institution of preferably active motion or at least fixation of the hand in the functionally correct position, are important. Penicillin is mentioned enthusiastically.

Wounds in the R.A.F. are classified into multiple foreign-body injuries in which healing is perfect and return to duty is permitted without the attempt to remove all of the embedded fragments, flak injuries, machine-gun bullets, cannon shell, and hand grenade and bomb explosion products. In these cases severe

injuries seem to predominate, ranging in gravity all the way up to cases in which whole parts of the body are blown away or must be immediately amputated, and in which resuscitation itself becomes a major problem. However by means of early surgical attention, a more generous use of immobilization with plaster casts, chemotherapy (penicillin seems likely to alter the established principles for the treatment of war wounds), conservative excision, adequate drainage and early rehabilitation, some surprising recoveries have been attained. In the air force amputations are delayed when possible, as the injuries are so apt to be multiple.

Seventy-five per cent of the cases of frostbite in air-crews are mild and recover rapidly. In most cases exposure of the affected part was deliberate and careless mechanical failure of the oxygen supply or of the heating accounted for some of the cases. Remarkable reduction in the incidence of frostbite in the air-crews, amounting to virtual abolition, has been achieved gradually by preventive measures, education, and technical improvements. Recent experience in the R.A.F. supports the view that elevation of the limb, avoidance of trauma, and cooling of the affected parts lead to the minimal loss of tissue. Cooling of the frostbitten part can be achieved by means of ice packs, a stream of cold air from a fan, or iced saline packs. Better still, however by simple exposure to room temperature.

In immersions the injury sustained depends upon the temperature of the water, the length of time of exposure, and the associated trauma; however there is usually added the general effects of exposure, and concomitant shock. The feet, ankles, and legs are the parts most commonly involved. Treatment consists in general measures to combat shock, elevation of the affected limbs, cooling by exposure to room temperature and surgical cleanliness.

A study of head injuries sustained in flying in members of air-crews reveals some interesting points, during the first two years of the war 1,515 cases were recorded. Head injuries alone or in association with other perhaps multiple injuries, but without maxillofacial involvement, accounted for 75 per cent of these patients. Maxillofacial injuries, on the other hand, were relatively rare, accounting for only 16.6 of the total of 1,545 injured. The combination of head and maxillofacial injuries was equally small, comprising 16.6 of a total of 748 survivors. None of the maxillofacial injuries proved fatal. On the whole the heaviest mortality has been in cases of skull fracture, especially when complicated by other injuries; however of the patients who survive the immediate effects, about 74 per cent are returned to flying duties, the majority within a period of two months or less. These results compare favorably with the end results of other injuries.

On the whole the advances made in the treatment of injuries of all kinds, as sustained by fliers, seem due to provision for the earliest and best possible treatment. Facilities provided by the Royal Air Force for its air-crews in special surgical depart-

ments for injuries resulting from flying and from enemy action exceed even those of teaching hospitals in peacetime. The final aim and object is to obtain the maximum operational efficiency in the shortest possible time. JOHN W. HAYNSMAN, M.D.

OPERATIVE SURGERY AND TECHNIQUE POSTOPERATIVE TREATMENT

May 11: Closure of Defects of the Lips with Composite Vermilion Border-lined Flaps. *Surg.* 1944 130 214.

Defects of the lips not suitable for direct closure may be repaired by the rotation of composite vermillion border-lined flaps. Vertical lip defects may be repaired in accordance with the principles of Eastlander's operation which is particularly adaptable for closure of triangular defects of the lower lip. The flap is pedicled and contains the coronary artery. To overcome vertical shortness and to enable full opening of the mouth, an additional operation is necessary. This requires the switching of triangular flaps. Defects of the lower lip and chin are best repaired when they appear triangular in form (Burrow) or heart-shaped (Dieffenbach). Triangles of skin and muscle are excised from the nasolabial region with the base of the triangle in line with the vermillion border. The mucous-membrane floor is incised and, if necessary, turned outward to lengthen the vermillion border. The cheek flaps are mobilized by means of an incision along the gingiva buccal sulcus which is carried to the anterior border of the masseter muscle. These flaps are then anchored into

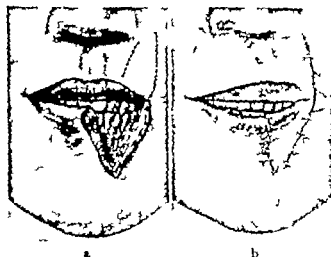


Fig. 2. a Triangular defect of the lower lip not larger than one-half the width of the lip. The defect includes the lower border of the left corner of the mouth. To close the defect, a vermillion border-lined flap is to be rotated from the upper lip and the nasolabial region. The pedicle of the flap containing the coronary artery is to replace the corner of the mouth. The flap should be made one-half as wide as the defect in order to shorten the upper and lower lips proportionately. b The flap is rotated into the defect. The secondary defect is closed by suturing the wound edges together.

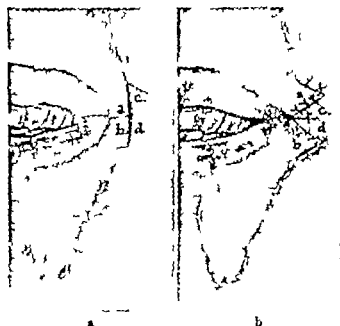


Fig. 3. a Reconstruction of corner of the mouth in those cases in which the pedicle of the flap (Fig. 1) forms the new corner of the mouth. The vertical shortness is overcome by switching triangular flaps. Flap (a) is exchanged with flap (c) with flap (b). Thus not only the oral orifice is widened, but a more natural corner of the mouth is achieved (Courtesy of J. B. Lippincott Co.).

position with oblique sutures to the gums. This is followed by closure of the triangles in layers, formation of the vermillion border and connection of the flaps in the midline. Finally the wound is drained from the lower vertical edge.

Large irregular defects involving the entire lower lip and chin are best closed by means of lined flaps from other parts of the body. If the defect can be made triangular, a modification of Dieffenbach's operation is recommended.

BENJAMIN G. P. SHAPIROFF, M.D.

Young, P. and Pavata, B. V.: Suture of Wounds by Plasma Thrombin Adhesion. *Br. J. Med. Chik.* 1944 6 80.

This report is an evaluation of the efficiency of plasma clot as a means of artificially producing rapid adhesion of wound surfaces. The method has been used in traumatic lacerations in which there is little or no tension on the wound edges as a skin suture in clean surgical incisions to promote adhesion when large wound surfaces are in contact, as in radical mastectomy and as a means of fixation of free skin grafts.

This method is a simulation of the normal process of wound healing. The formation of fibrin occurs early in clean wound healing. The fibrin acts as a binding agent between the wound surfaces.

Over a period of years various investigators have studied the use of plasma clot as a suture material. It has been found effective but to have less tensile strength than the usual fine sutures of silk or surgical

gut in common use. The main disadvantage when the plasma was allowed to clot spontaneously or when this action was accelerated by various tissue extracts was the slow formation of the clot. Consequently progress has been made in the purification and isolation of thrombin and through its use rapid clotting of plasma can be obtained. In fact the speed of clot formation can be adjusted as desired by varying the concentration of thrombin used. Moreover, since thrombin was found to be nontoxic when applied to the surfaces of wounds, it can be safely used for fibrin suture.

The artificial formation of fibrin in wounds is simple. The surfaces of the wound are first flushed with plasma. It is not necessary that the plasma be autologous. The plasma used has been the stock pooled plasma from a plasma bank. Excess is avoided since this will result in a gelatinous mass of clot which on contraction releases an undesirable amount of fluid.

After plasma has been evenly distributed over the wound surfaces, thrombin solution of the desired concentration is sprayed on the wound with syringe and needle. The surfaces of the wound are quickly adjusted and held in apposition steadily and evenly for about two minutes or for a period of about twice as long as is necessary for fibrin to form from the solution of the strength being used. It is important to realize that any movement of the wound surfaces or edges during this part of the procedure will result in failure of adhesion. Time must be given for the thorough precipitation of fibrin and its attachment to the wound surfaces. As previously mentioned the tensile strength of plasma clot is not great. After a few minutes have elapsed for fibrin formation one can exert moderate pull on the wound without the occurrence of separation. If greater pull is exerted, one can see the fibrin strands stretch and finally rupture. It is therefore usually advisable to support wounds sutured in this manner by compression dressings and to prevent motion for a few days. Motion should not be allowed too soon since the healing process can be disrupted even up to fourteen days.

Adherence of wound edges or surfaces can be readily accomplished by the use of plasma and purified thrombin. The fibrin fixation artificially produced in this way has less tensile strength than ordinary suture material for this reason use of plasma-thrombin adhesion of wounds should be limited to those wounds in which tension does not exert.

Plasma thrombin adhesion has been found useful (1) as the sole fixation for traumatic lacerations (2) as a skin closure where a particularly fine scar is desired (3) as a method of producing adhesion between the flaps and the chest wall in radical mastectomy and (4) as an adjunct in free skin grafting.

No untoward results have been observed in 60 cases in which the plasma-thrombin method of adhesion of wounds has been used.

JOHN L. KIRKPATRICK, M.D.

Collier F. A., Crook, C. E. and Job, V.: Blood Loss in Surgical Operations; Chairman Address. *J. Am. M. Ass.* 1944 86 1

The amount of blood lost during surgical operations of various types has been measured and reported by a number of observers. The facts disclosed by these observations have not been generally recognized nor has their practical importance been sufficiently emphasized. In order to bring attention to this technical problem, the literature on it has been reviewed and further studies have been made and are here reported. Shock appearing during and after operation is still the apprehension of the surgeon and a menace to the patient. During the past three years an enormous amount of investigation on the subject of shock has added materially to our knowledge of it. One fact, however, remains clear there is no single reliable test or clinical sign of impending shock especially in anesthetic and postanesthetic state. By the time shock is recognized as such it is well established. Our ability to treat shock has improved but it is far from satisfactory. The earlier the treatment is instituted the better the results, and if its advent is anticipated it may be prevented far easier than it may be cured. Though there are no positive early tests of impending shock there is a large body of ground of clinical observation from which to deduce that shock will appear under certain circumstances—burns involving 30 per cent or more of the body surface, severe dehydration, multiple fractures or wounds, crushing injuries, exposure to cold air or immersion in cold water and extensive blood loss. It is well known that shock develops more readily after a given injury if there exists malnutrition or starvation, anemia, dehydration, physical or mental exhaustion, chronic illness, or prolonged bed rest. With these facts available, one should be able to anticipate and usually prevent shock in the surgeon in civilian hospitals.

In 1924 Gatch and Little reported the first study of blood loss during some of the more common operations in general surgery in which accurate measurements of the losses were made. They pointed out that the amount of blood lost in the ordinary laparotomy is not great but that in operations involving extensive dissection the loss may be excessive. They concluded that a patient in fairly good physical condition could lose from 600 to 700 cc. of blood without any apparent harmful effect on the postoperative course. Likewise an adult in good health does not manifest any serious effect from hemorrhage until the amount of blood lost is between 800 and 1,000 cc. Alexander Blain in 1929, in commenting on his experience with 3,000 transfusions, stated that the amount of blood lost at operation is often several times greater than that estimated by the surgeon. He urged the preoperative correction of anemia and the immediate replacement of blood lost during operation and condemned delay in giving blood transfusions until after shock had developed. Collier and Maddock in 1932 measured blood loss during some of the ordinary operations and con-

cluded that the amount of blood lost is always greater than the surgeon estimates. Windfeldt in 1937 made direct measurements of blood loss during operations and concluded that the loss is often far greater than supposed so that without appearing dangerous it may reduce the volume of the circulating blood considerably. Determination of hemoglobin concentrations before and after operation did not give quantitative information regarding the amount of blood lost. Pilcher and Sheard in 1937 estimated the blood loss by a photometric method and found that the average loss from prostatic resections was 49 cc. This finding stimulated efforts to secure better hemostasis and in a second series studied after alterations were made in the technique, the average loss was reduced to 391 cc. A group of 49 general surgical cases was studied for comparison. Hubby in 1937 used this method to determine the hemostatic effect of congo red. White, Whitlaw, Sweet and Hurwitt in 1938 made an exhaustive study of blood loss in neurosurgical operations. They found that in the course of extensive intracranial operations the average loss was from 500 to 1,500 cc. They concluded that these patients rarely develop the typical shock state unless the loss is over 1,200 cc. or unless the loss is rapid. They urged greater attention to hemostasis at the expense of time and advocated discontinuance of the operation if the loss exceeded 1,200 to 1,500 cc. Stewart and Rourke in 1938 studied changes in the blood and interstitial fluid resulting from surgical operation and ether anesthesia. They pointed out that the hematocrit changes induced by trauma and blood loss of operation are not proportional to the blood loss and that the structurally important elements of blood plasma, that is, protein, sodium and chloride are accurately sustained by the body. They emphasized the fallacy of assuming a quantitative relationship between the changes in the concentration of hemoglobin or plasma protein and changes in the plasma volume.

Leriche and Vasilaros in 1939 reported measurements of the blood loss in 29 operations of diverse character. They concluded that a loss even as small as 500 cc. of blood is not a matter of indifference to a body which is called on to effect the repair of trauma and disease. Nesbit and Conger in 1941 measured the blood loss associated with transurethral prostatectomy and stated that this determination is easily carried out at the time of operation and should be made a routine procedure so that untoward blood losses may be immediately appreciated and corrected by transfusion. They urge the use of whole blood to replace the blood loss accurately. Wangenstein in 1942 described a gravimetric method for determining the status of hydration and blood loss during operation. He advocated the replacement of minor blood loss by an amount of plasma from 100 to 200 cc. greater than the blood lost, or if the loss is excessive it should be replaced by whole blood. He found the average blood loss from gastric resection to be from 300 to 500 cc. In 1942 Buxton and White measured the blood loss in 109 patients

undergoing operations on and in the thorax. The loss in these operations was exceptionally large, averaging about 700 cc. for each stage thoracoplasty, 1,600 cc. in lobectomy, and about the same for pneumonectomy. Large transfusions during operation were advised. Oppenheim, Pack, Abels and Rhoads in 1944 measured the amounts of blood lost in various abdominal operations and described a simplified method for carrying out this technique. The amount of blood lost was not excessive. However they believed that a transfusion of from 500 to 600 cc. of blood during the operation is of great benefit to patients operated on for cancer of the gastrointestinal tract. They advised the routine determination of blood loss, especially in elderly patients with cardiovascular insufficiency in order to prevent the administration of unnecessarily large amounts of fluid.

In table I in the original article are shown the blood losses from 626 operations collected from the data of these authors. The cases are grouped according to the types of operation and the maximal minimal and average losses are given. It was the unanimous conclusion of all who studied this problem that the blood losses in nearly every operation were greater than expected by the surgeon. The constant ooze of blood from large vascular fields leads to a large loss of which the surgeon is frequently not cognizant. Accurate measurement of blood loss leads to an appreciation of the importance of better hemostasis. Nevertheless at times in spite of every effort at hemostasis the loss will still be large and transfusions should be planned in advance.

Analysis of the literature impresses one with the fact that not enough emphasis has been placed on the relation of the amount of blood lost to the total blood volume. Since the blood volume varies with the weight of the patient, it makes a vital difference whether a given amount of blood is lost from a large adult or from a small child. In table 2 are shown some figures illustrating the relationship of a 100 cc. blood loss to the blood volume in patients of differing weights. Blood comprises 77.7 cc. per kgm. of body weight in the male and 66.1 cc. per kgm. in the female. For all practical purposes one thirteenth of the body weight is blood and cells make up 45 per cent of the blood volume in men and 40 per cent in women. A simple method of calculating blood volume is to allow 30 cc. of blood for every pound or 75 cc. for each kilogram of body weight. Stewart and Rourke showed blood loss in terms of percentage of total blood volume but did not comment on its critical relation to weight. Nadal pointed out the important relationship between the size of the patient and the amount of blood that could be lost before signs of shock would appear.

Since several of the preceding studies were carried out in the University Hospital, Ann Arbor, Michigan, the surgical staff has come to realize the importance of a knowledge of blood loss during operation. Further investigations have been made to stress the necessity of admitting that blood will be

lost that its approximate amount should be known and that it should be replaced by blood. Fifty cases were studied and 42 have been selected for presentation. The method used for determining blood loss was essentially that of Gatch and Little with the following exceptions:

1. Oxyhemoglobin was measured in the Evelyn photoelectric colorimeter.

2. The fluid from aspirator bottle instrument and glove washings was kept separate from the washtub fluid.

3. The sample from the 50 liters of washtub fluid was taken directly from the washtub before the drapes and gauze sponges were removed. Controlled washings with known amounts of blood on sample outfits of drapes and sponges yielded an average recovery of 95 per cent. The detailed method was as follows:

With Evelyn's method oxyhemoglobin was determined on the solution containing equal volumes of the following fractions:

1. Fluid from drapes and sponges extracted in washing machine in 50 liters of distilled water for two hours.

2. Aspirated fluid and water used to wash instruments and gloves diluted to 5 liters or to 10 liters if necessary and finally diluted 1:10 or 1:5 with distilled water. The solution was centrifuged to clarify it and diluted 1:1 with distilled water.

The patient's preoperative concentration of hemoglobin was determined at the same time.

Calculations

Gm. Hb lost = C m % Hb from blood curve $\times \frac{1,000}{250}$

$\frac{\text{Hb lost}}{\text{pt's. preop. Hb}} \times 100 = \text{cc. blood lost}$

The cases here presented were selected for study on the basis that because of their character a high blood loss might be expected, and that they were limited chiefly to five categories to facilitate comparison. Particular interest was centered in changes in the blood picture associated with hemorrhage. Therefore many patients whose blood loss was minimal were excluded from the presentation. Consequently the blood loss in these groups does not represent average results from routine operations of their types. The operations were performed by ten surgeons from the resident staff.

In tables 3 to 8 are shown measured blood loss and its percentage of total blood volume. Intravenous solutions given in the operating room, blood transfusions given during or immediately after operation, and the degree of hypotension stated in terms of 1 to 4 plus in patients during various types of operation. In table 3 the blood loss from radical mastectomy is slightly higher than found by others but, since these operations are always accompanied by such losses, transfusion during these operations has been made a routine at the University Hospital by the staff. Patient 27 developed a moderate hypotension which was corrected by transfusion of blood equal in

amount to the loss. In table 4 the blood loss associated with thyroidectomy is shown. These patients all presented large recurrent, or unusually large goiters and the average blood loss was much higher than found in routine thyroidectomies. In 12 instances the loss was above 25 per cent of the blood volume but the surgeon realized this fact and replaced the lost blood by transfusion during the operation.

In table 5 is shown a group of patients presenting difficult technical problems in surgery of the biliary tract. Many had been operated on previously. The majority were jaundiced and in all the common duct was explored or reconstructed. The operations were long and the blood loss averaged nearly 600 cc. Case 41 is of interest since the blood loss of 1,065 cc. represented 41 per cent of the blood volume; the patient was emaciated and weighed only 46 pounds (39 kgm.). This patient developed an alarming shock state from the operative trauma, blood loss, and bile peritonitis, and was given 3,000 cc. of blood in the next forty-eight hours after which convalescence was relatively uneventful. Contrast this 41 per cent loss with that of case 21 in which a larger amount of blood, 1,455 cc., was lost, the latter amount representing only 27 per cent of the total blood volume. Both cases required extensive replacement by blood. In operations of this character performed on undernourished and jaundiced patients one should always plan on adequate replacement of the blood loss. The routine immediate replacement of blood in these patients was found to be inadequate at the time of the study and the authors have since planned for a liter of blood to be given during operation.

Table 6 presents studies of blood loss in 12 cases of cancer of the rectum treated by a single stage abdominal perineal resection. The losses in this group averaged 410 cc., the principal loss resulting from the perineal dissection. While this loss is not great it should always be replaced by blood as so many of these patients are malnourished, anemic, and dehydrated (Miles regimen). The occurrence of hypotension in these patients (case 26) was thought to be of anesthetic origin. Table 7 presents 3 complicated gastric resections accompanied by a blood loss averaging 600 cc. In table 8 is shown the relatively large losses resulting from operation in which large body surfaces are opened. This blood loss is from multiple small rather than from single large vessels. The use of gauze packs as hemostatic agents tends to obscure hemorrhage rather than control it. Table 3 is a similar example of operations on large body surfaces.

Concurrently with the blood-loss determinations, observations were made of changes in hematocrit and hemoglobin and plasma protein concentration before and after operation. These findings are listed in relation to blood loss in table 9 and deductions from them agree with those of Stewart and Rowntree. There was found no correlation between the amount of blood lost and the simultaneous changes in hematocrit, hemoglobin, and concentration of plasma

protein immediately before and following operation.

These determinations therefore cannot be used to estimate the need for blood volume replacement during and after operation. Obviously, it follows that if one wishes to know the amount of blood lost in any operation one must depend on direct measurement. This approach is not often practical, in which event one must rely primarily on a knowledge of average losses to provide a basis for the replacement of blood loss during operation. Additional blood may be given if the clinical state of the individual demands it.

The authors believe that even minimal blood loss retards convalescence; that all loss over 300 cc. in healthy adults should be replaced; and that all blood loss in operations on aged, undernourished, seriously ill, or bedfast patients should be replaced with equal quantities of blood.

JOHN J. MALONEY, M.D.

McClure, R. D., Warren, K. W., and Fallis, L. S.
Intravenous Pectin Solution in the Prophylaxis and Treatment of Shock. *Canad. M. Ass. J.* 1944, 51, 206.

Pectin solution was administered intravenously as a blood substitute to 275 patients. In the majority of cases it was given prophylactically during some major surgical procedure on the gastrointestinal tract. All solutions were carefully prepared by the method of Hartman and were tested for osmotic pressure, viscosity, specific gravity, and pH. The importance of carefully controlled preparation of the solution is emphasized. The amount of solution administered varied between 200 and 1,600 cc. with the most frequent dose being 800 cc. Results were evaluated by the course of the blood pressure and pulse during operation and by the presence or absence of shock postoperatively. Measured by these standards the results were good in 75 per cent, fair in 20 per cent and poor in 5 per cent of the patients.

The untoward effects of pectin administration are discussed. Rouleaux formation follows and persists for at least twenty-four hours but causes no detectable symptoms. The sedimentation rate rises in all cases. Only 2 patients in a series of over 300 manifested any evidence of reaction. Purpura was not observed with dosages suitable for the prophylaxis of shock, although it occurred following large daily doses for other purposes. Tissue deposition has been reported following the administration of more than 4,000 cc. of commercially prepared pectin.

It is concluded that pectin, though inferior to blood or plasma, appears to be of more value than glucose or saline solution in the prophylaxis of shock in extensive surgical procedures. It is nontoxic and nonantigenic in quantities of from 1,000 to 1,500 cc., which are usually required to maintain the blood pressure in the presence of shock-producing conditions. Untoward effects appear only after the intravenous injection of amounts in excess of 4,000 cc.

JOHN L. LINDQUIST, M.D.

ANTISEPTIC SURGERY TREATMENT OF WOUNDS AND INFECTIONS

Byrne, J. J.: Grease-Gun Injuries. *J. Am. M. Ass.* 1944, 135, 405.

A case presented by Smith is discussed in which grease was accidentally injected into the base of the left index finger under 7,000 pounds of pressure. The subsequent course is followed. Two cases reported by Brooke and Rooke and 2 cases reported by Mason and Queen are abstracted in this article.

The author presents the case of a man who accidentally had grease injected into his left 4th finger. The subsequent clinical and laboratory findings are presented and discussed very fully and practically a day-by-day follow-up of the case is given. The author believes that pressure, chemical irritation of the grease, and secondary infection are the three factors which may devitalize tissue in the acute phase of this type of injury. If the original pressure does not cause irreparable damage, the grease may act further as an irritant and set up subsequent acute reactions. In the chronic phase of these injuries, most of the grease is encapsulated in chronic inflammatory tissue or may be slowly removed by phagocytosis. Encapsulated grease may not remain inert in the tissue but may cause a formation of tumors. Microscopic examination of these tumors reveals whorls of fibroblasts with foam cells, plasma cells, polymorphonuclear cells, and some lymphocytes, monocytes, and giant cells.

The best treatment is prophylactic. Once an injury has occurred, expectant and conservative treatment should be followed in the form of bed rest, sedation, and massive dressings at room temperature. No hot dressings should be used as this may lead to gangrene. Longitudinal incisions are of doubtful value in removing the widespread grease. Surgery should be limited to the removal of sloughing tissue and/or incision of fluctuant areas when abscesses develop. Early amputation is not recommended. A general anesthetic is recommended. Procaine digital block is condemned. Subcutaneous oleomas should be removed under a general anesthetic in a bloodless field. When overlying skin is involved, it should be sacrificed and the resultant defect repaired with free or pedicled skin grafts.

RICHARD J. BENNETT, JR., M.D.

Dingwall, J. A., III., and Andrus, W. DeW.: A Comparison of Various Types of Local Treatment in a Controlled Series of Experimental Burns in Human Volunteers. *Ann. Surg.* 1944, 120, 377.

In order to evaluate the efficacy of 12 different local treatments of burns, the authors have produced 82 bilateral, symmetrical burns in 41 human volunteers with the use of a simple apparatus consisting of a hollow metal plate of almost exactly 10 square centimeters of area through which live steam is passed. When such a device of constant temperature and area is applied to symmetrical points on the anterior

a part of the thigh for the same length of time as determined by an electric timer by which tenths of second were easily measured the resulting burns should be very nearly alike in every way including depth. As proved by biopsy the fluorescein test and by the nature of the subsequent healing process of uncomplicated lesions these areas were deep second degree burns. Without fail all lesions showed vesiculation in twenty-four hours.

For the twenty-four hours following the production of these lesions dry sterile gauze was used as a covering, it was secured by adhesive tape and completely closed the areas. The twenty-four hour delay before the administration of definite therapy was chosen in order to stimulate accidental burns since these were frequently seen after some time had elapsed. Following removal of the initial dressing, all vesicles were opened under sterile technique and the areas were debrided in the majority of instances. Routine cultures were taken at this time. One burn was then selected at random for definite therapy with one agent and the contralateral area was used as a control, a different therapeutic preparation being employed.

The result of the following treatments were studied: sulfafilm control film (without sulfonamides) tannic acid boric acid ointment, boric acid ointment combined with the oral administration of sulfadiazine triple dye vaselined gauze triethanol amine sulfadiazine with methocel penicillin ointment fibrin film and sulfadiazine gelatin.

The best results as measured by the rapidity of healing absence of symptoms and freedom from all complications were encountered in the group treated with a sulfonamide-impregnated plastic film. The next best method of treatment, which was very nearly as efficacious was the local administration of a bland ointment combined with the oral administration of sulfonamides.

The value of the use of the sulfonamides either locally or systemically was clearly demonstrated in the control of infection while the evidence of sensitivity resulting from their local application was minimal, and believed to be of no practical significance.

The importance of restricting the frequency of dressings was confirmed as there was a direct relationship between the rate of healing and the number of times the dressings were removed. Under the conditions of the experimental series the lesions which were not debrided healed as well and as rapidly as those from which all nonviable tissue was carefully removed.

The authors' experience in this series of experimental burns gives additional evidence for the abandonment of any type of treatment with escharotic agents.

The authors suggest that so-called second-degree burns should be carefully described as to their depth to facilitate greater accuracy in comparing the results obtained in series reported in the literature.

JOSEPH K. NARAY, M.D.

Gardiner, R. H.: Intraperitoneal Chemotherapy. *Br J Surg* 34: 37-49.

No method of effectively combating peritonitis by a direct attack had been devised before the introduction of the sulfonamide drugs which are successful in a large majority of cases if used intraperitoneally. Diversity of bacterial flora and the presence of a large quantity of free pus interfere with the action of the sulfonamides in peritonitis.

Sulfanilamide and sulfapyridine appear to be the drugs of choice and sulfapyridine shows the slowest absorption rate and the lowest toxicity of any so far employed. On the average, 15 gm. is the dose of the sterilized powder recommended, but 25 gm. or more may be inserted if profuse suppuration is present.

Contaminated wounds treated with an emulsion of sulfonamide powders will heal by first intention in the large majority of cases.

Intraperitoneal chemotherapy should now be included in the armamentarium of all emergency surgeons. This is borne out by the reports showing a fall in the mortality rate of appendicitis and its complications, and other acute abdominal conditions when it is employed.

Encouraging results appear to accrue from its use in intestinal obstruction necessitating bowel resection but further investigation is necessary.

The whole course of large bowel surgery may be altered by the use of intraperitoneal chemotherapy and the axial anastomosis become a safe method and the one of choice for the reconstitution of bowel continuity. Care in diagnosis, preoperative and postoperative treatment and technique is essential, and chemotherapy is only an adjunct to these.

HOWARD A. MCKENRY, M.D.

Ellis, F. A.: The Potential Danger of the Topical Use of Sulfathiazole; Report of 16 Cases of Sensitization to Sulfathiazole. *Sent. M J* 1944 37: 493.

Within the last year Ellis has seen 16 patients who were thought to be sensitive to sulfathiazole locally or internally. Fifteen gave positive patch tests to sulfathiazole ointment and 1 was not tested because the generalized eruption did not clear up sufficiently before the patient was lost from observation. 7 patients developed a generalized dermatitis immediately following the ingestion of sulfathiazole. Later 1 took sulfadiazine without difficulty.

It has been suggested that sulfathiazole ointment should not be used for more than five days and that the use of this ointment in eczematous eruptions without infection is of no value but is prone to sensitize the patient to sulfathiazole. The local use of sulfonamides may sensitize the individual and perhaps later preclude internal sulfonamide therapy in far graver diseases. This form of medication should be used only for short periods and then only when there is an active pyogenic or other infection which is known to respond to local sulfathiazole therapy.

There is some evidence that a vehicle containing lanolin or cholesterol compounds may increase the

possibility of sensitization to sulfathiazole and to the base. The use of band-aids impregnated with sulfathiazole as recommended by several reliable pharmaceutical firms may cause more harm than good. The local use of proprietary medicaments containing the sulfonamides is also dangerous and should be prohibited. Intranasal therapy with solutions of sulfathiazole may sensitize the patient.

J M MOXA, M.D

Kirby W M., and Hepp V E.: Treatment of Osteomyelitis of the Facial Bones with Penicillin. *J Am Med Ass* 1944, 125 1019

In spite of sulfonamide therapy osteomyelitis of the facial bones either as a postoperative complication or as an extension from diseased sinuses results in a mortality of 80 per cent particularly when there is associated infection of the brain and meninges.

After seeing a small series of cases the author recommends that the patients be treated exclusively with penicillin for a period of from three to four weeks until sequestration of the devitalized bone is complete. Prolonged treatment with larger doses of penicillin is more effective than treatment with smaller doses which was usually followed by relapses. The dosage of penicillin recommended is 500,000 units daily given by continuous intravenous drip for from ten to fourteen days. Thereafter 15,000 units are administered intramuscularly every three hours for from fourteen to twenty-one days. The sequestra are then removed surgically and penicillin therapy is continued for seven postoperative days.

The organisms responsible for the osteomyelitis of the facial bones in this series were the anaerobic non hemolytic streptococci and the coagulase positive staphylococcus aureus. This combination of penicillin therapy and surgery appeared to cause a drastic reduction of the mortality rate.

BENJAMIN G P SHAFIROFF M.D

Jeffrey J S., and Thomson S.: Penicillin in Battle Casualties. *Brit Med J* 1944, 2 1

This report summarizes the effect of penicillin in the treatment of soldiers wounded on the Italian front from January to June 1944. Penicillin was used at a few selected forward stations in the forward area. In place of sulfanilamide a mixture of penicillin-sulfathiazole powder (5 000 units of penicillin per gram of sulfathiazole) was insufflated into the wound. The recognized surgical principles of wound treatment were in no way abandoned.

In one series of cases 50 per cent of the debrided wounds insufflated with penicillin showed no growth on culture at the base five days later. The technique of penicillin insufflation varied with the nature of the wound. Dirty superficial wounds received one daily insufflation for two days and were then sutured on the third day after frosting with the powder mixture. Perforating wounds were sutured with fine rubber tubes leading down into the sinus and 3 cc. of penicillin (250 units per cubic centimeter) were instilled through each tube for four days.

One base hospital reported that there were no failures when 110 superficial wounds were sutured and given one insufflation of penicillin sulfathiazole powder. From the same hospital failures were reported in 23 per cent of 68 superficial wounds sutured after the application of sulfanilamide.

Twenty five cases of large shell wounds of the buttocks or thighs were treated by suture and drainage tubes through which insufflations were made. As a result of this form of treatment, 70 per cent of the wounds healed in ten days. Previously the healing time was at least forty days.

Penicillin was found to be of great value in the management of hemothorax or empyema. For these conditions local instillations into the pleural cavity were essential because systemically the penicillin did not get through the pleural barrier in sufficient concentration. If the treatment consisted of aspiration alone 60,000 units of penicillin dissolved in from 30 to 60 cc. of water were instilled at the end of aspiration. With this method of treatment the incidence of rib-resection operations for empyema decreased.

Gas gangrene which usually resulted in a 50 per cent mortality was reduced to 25 per cent when penicillin was used in combination with surgery and antiserum. Penicillin was also found to be superior to the sulfonamides in the treatment of head wounds involving the scalp and brain. It was not used in the treatment of penetrating wounds of the abdomen because it was believed that physiological causes were responsible for the high percentage of deaths rather than infection.

BENJAMIN G P SHAFIROFF M.D

Hepl, M., Ochauer A. and Dixon J L.: Two Cases of Clostridium Welchii Infection Treated with Penicillin. *J Am Med Ass* 1944, 26 96

The development of gas gangrene in a traumatic wound depends on four factors: (1) contamination of the wound with soil or foreign bodies containing clostridia; (2) inadequate blood supply to the affected part; (3) inadequate debridement; and (4) conditions in the wound for anaerobic growth. A combination of these four factors in a given patient will almost invariably give rise to clinical gas gangrene.

Once clinical gas gangrene has fully developed the only known treatment is radical surgery, laying the affected parts wide open and many times of necessity doing a high guillotine amputation in order to save the patient's life.

Any chemical or biotic substance which will inhibit the growth of clostridia in traumatic wounds would be of inestimable value in saving limbs and lives.

The discovery of the action of penicillin and its use in experimental clostridium welchii infections held promise that this drug would be of value in such infections. As animal experiments are inconclusive in regard to human therapy it remains for the clinician to put penicillin to the final test in regard to its efficacy in the treatment of gas gangrene.

Of 2 cases of clostridium welchii infection one was treated locally with calcium penicillin and the other systemically with sodium penicillin and locally with calcium penicillin. Careful bacteriological studies showed persistence of the clostridium welchii in the case of cellulitis treated with calcium penicillin locally while the use of penicillin systemically and locally combined with guillotine amputation caused the disappearance of the beta-hemolytic streptococcus and the clostridium welchii from the spreading infection. After the oral administration of sulfadiazine beta-hemolytic streptococci could not be recovered from the blood stream. It must be emphasized that good surgery was the deciding factor in the second case, and that penicillin is of most benefit when used in conjunction with good surgical principles.

J. M. Mora, M.D.

ANESTHESIA

Hudson, F.: Four Hundred and Ten Cases of Goiter Under General Anesthesia with Pentothal. *Current Res Anesth* 944 23 211

Four hundred and ten cases of goiter were anesthetized with sodium pentothal at the Hotel Dieu in Quebec. Preoperative medication included 1½ mgm. of nembutal the night before and ¼ gr. of morphine with 1/150 gr. of atropine one hour before surgery. Two and one-half per cent solution of pentothal was given by means of the Luer Lok syringe on a tubing and the Luer Lok adapter to the needle. From five to eight minutes were allowed to put the patient to sleep meanwhile doses of 100 mgm. or 5 cc. were injected at a time. Laryngoscopic airways were kept available for emergencies. Pentothal was found to lower the metabolism, the pulse and respiration gradually becoming slower during the operation.

Four men died after the operation, one of cardiac syncope the day following, a second from bronchopneumonia on the fourth day, a third also from bronchopneumonia and a fourth from tracheal compression from a large hematoma plus cord spasm caused by the irritation. Atropine was given to avoid laryngeal spasm. Oxygen was used at the slightest sign of cyanosis and morphine doses were held down to a minimum.

The author believed that pentothal sodium was indicated in the toxic thyroid because it decreases the metabolism, is well tolerated by the patient and considerably lowers the postoperative hyperthyroid crisis.

MARY KARP, M.D.

Adams, R. C.: Pentothal-Sodium Intravenous Anesthesia in Peace and War. *J. Am. M. Ass.* 944 26 28

This month marks the end of the first decade since the clinical introduction of pentothal sodium. During each of these ten years the use of this anesthetic has increased generally throughout the country and in each year changes in our attitude toward its use, its scope, and its administration have occurred. It is

now known that it is not detoxified by the liver or kidneys and does not affect the metabolic process of the body in general. It can be used with safety when the solutions have been mixed for as long as forty-eight hours. It is usually administered in a 2.5 per cent concentration. Its margin of safety is wide. Workers with the drug vary in their opinion as to its scope of usefulness. The author discusses its administration for intra-abdominal operations and for operations in regions in which the reflexes are particularly hyperactive such as the nose, throat, larynx and anal region. He questions the advisability of using it for operations of this type. He suggests the administration of oxygen throughout, with oxygen and nitrous oxide in 50-per cent concentration.

The field of usefulness of pentothal sodium has been extended to various methods of anesthesia and it is recommended in conjunction with local infiltration block anesthesia, and local anesthesia in the very nervous patient, and to supplement local anesthesia that is wearing off or that has not been adequate. It is also recommended in a combined technique with block of the abdominal wall, or later costal block for abdominal operations. It has been used for induction in an inhalation or as either anesthesia and in combination with topical anesthetics.

Its contraindications include very young children, patients with degenerative diseases of the myocardium particularly if dyspnea is present, and operations in which the integrity of the airway cannot be assured.

The simplicity of equipment, the ease of transportation and the fire-proof qualities of this substance have caused its use in World War II to be an enviable one. It is now believed that it can be used in the shocked patient if smaller doses are administered if shock is controlled when possible before anesthesia is begun. If consideration is taken of the amount of morphine which has been given before the administration of this drug and if airways and oxygen equipment are available. An anesthetist trained in the uses of the method and the effects of the drug is important to its safe administration. Its wartime usefulness includes its administration for preliminary débridement of bomb-burned victims and persons who have sustained minor war injuries. When shock was minimal, intravenous anesthesia did not appear to aggravate the shock further. The drug is not contraindicated when patients are undergoing treatment with the sulfonamide compounds. The total dosage varies from 1,000 to 2,000 mgm. The value of the method in military surgery up to the present phase of World War II is rather gratifying.

MARY KARP, M.D.

Lettimon, W. T. and Heger, H. G., Jr.: Continuous Spinal Anesthesia: Observations on 2,000 Cases. *Ann. Surg.* 1944, 120 129.

The observations and impressions in 2,000 continuous spinal anesthetics are reported by the authors. Because of its low toxicity procaine hydro-

chloride was the agent used in all but 1 case. The advantages of the method include the ability to obtain an adequate length of time and an adequate level of anesthesia. Aspiration of the spinal fluid containing the drug promotes rapid recovery from the effects of the drug.

The technique of administration was described in detail with stress on the need for making and maintaining a good puncture. Preliminary medication consisted of the hypodermic injection of morphine sulfate (gr $\frac{1}{4}$) and scopolamine hydrobromide (gr $\frac{1}{100}$) one hour before operation. Subsequent doses of morphine were given as the need for sedation exerted itself. If the preliminary doses of ephedrine had been given with procaine for skin anesthesia it was seldom necessary to add vasomotor drugs during the course of anesthesia or operation. Among the 2,000 cases only 3 were unsatisfactory. One patient developed uncontrollable coughing during the course of a pulmonary lobectomy. Faulty technique caused failure in the 2 other cases.

The ages of the patients varied from two days to eighty-seven years. The authors found the procedure very satisfactory in children, the success depending upon the liberal use of morphine in multiple small doses. The total dosage per case averaged 310.9 mgm., the smallest dose being 20 mgm. and the largest 2,200 mgm. Five per cent solution of procaine in spinal fluid was used. Additional doses were prepared in sterile distilled water or normal saline solution. The incidence of headaches following continuous spinal anesthesia was about the same as that following the use of single-dose spinal anesthesia, and averaged about 3.1 per cent. The incidence of urinary retention was 3.3 per cent, not including the cases in which it was prolonged and indwelling catheters were used. Forty-five cases of pulmonary complications occurred. Twenty-seven of these were bronchopneumonia, 11 lobar pneumonia, 5 atelectasis, and 2 pulmonary embolism. One patient developed anesthesia of the upper lip, this disappeared in two days. No other neurological complications occurred.

The authors strongly recommend the procedure because of its adequacy, safety, and controllability.

MARY KARP, M.D.

Hilnebaugh, M. C., Jr., and Lang, W. R.: Continuous Spinal Anesthesia for Labor and Delivery. A Preliminary Report. *Ann Surg* 1944 120 143.

A malleable steel needle of the type used by Hingson and Edwards is inserted into the subarachnoid space through the first and second lumbar interspace for continuous spinal anesthesia during labor and delivery. The agent used is 1.5 per cent metycaine in Ringer's solution. The standard dose is 1 cc. or 15 mgm., repeated as necessary usually in from twenty-five to forty minutes. The height of anesthesia should be 2 or 3 cm. above the umbilicus. Any additional height may cause the danger of cessation of the uterine contractions. The dosage given was adequate to produce anesthesia but com-

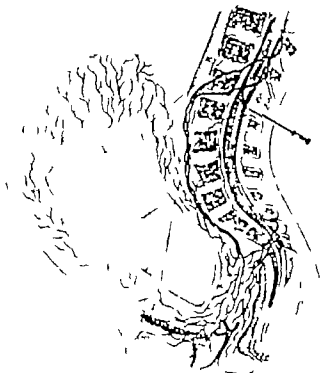


Fig. 1. Sagittal section of a pregnant woman showing spinal needle in place between the first and second lumbar vertebrae. Note the needle's proximity to (1) the eleventh and twelfth thoracic nerves which carry uterine sensory fibers, and (2) the second, third, and fourth sacral nerves which carry sensory fibers from the cervix and lower birth canal.

Puncture of the dura at a higher level might result in injury to the spinal cord. Motor fibers, not shown, are involved if the anesthesia blocks the sixth or higher thoracic nerves. (Courtesy of J. B. Lippincott Co.)

plete motor paralysis did not occur. The needle was withdrawn when the patient was placed on the delivery table although the authors believe that a split mattress would make it possible to permit the needle to remain *in situ* during the entire delivery.

Complete relief of pain was obtained in 40 cases, or 80 per cent, and partial relief was obtained in 8 cases, or 16 per cent. In 2 cases the anesthesia was a complete failure. Twelve per cent of the patients required inhalation anesthesia for delivery. Dislodgment of the needles occurred in 3 cases. The labor did not appear to be lengthened. The cervix should be dilated 4 cm. and completely effaced before the method is instituted in the nullipara. A dilatation of 3 cm. is satisfactory in the multiparous woman. There was no interference with the frequency and force of the uterine contractions. Cervical dilatation seemed to be accelerated. The normal mechanism of second-stage labor was in most instances delayed. Ninety-eight per cent of the

cases had operative intervention in the second stage 56 per cent by low forceps and 12 per cent by mid forceps. Midforceps seem to be the rule in occiput posterior positions because the relaxed pelvic floor permits extension of the head with resultant arrest. The third stage proceeded normally. No case of retained placenta occurred. There was less bleeding than when other methods were used. Ninety per cent of the mothers reacted favorably to the method and were enthusiastic over the relief of pain. No alteration of the blood pressure occurred.

Twenty-two women, or 42 per cent, experienced rather severe but transient headaches which were relieved by mild analgesics. No adverse effect was found to occur upon the fetus. The indications include prematurity, heart disease, hypertensive toxemia, pulmonary disease and previous cervical, and vaginal repair. Contraindications include deformity, local infection, marked obesity, sensitivity to the drug, emotional instability, severe anemia, non-engagement of the presenting part, cephalopelvic disproportion, known fetal deformity, placenta previa, and internal podalic version.

The method is time-consuming and requires constant personal supervision. It is both unfair and dangerous to give the initial injection and place the responsibility for its continuation in the hands of an intern or nurse.

MARY KARP, M.D.

Ivy, A. C., Goetzl, F. R., and Burrill, D. V.: Morphine-Dextroamphetamine Analgesia: The Analgesic Effects of Morphine Sulfate Alone and in Combination with Dextroamphetamine in Normal Human Subjects. II. *Med. Chir.* 1944, 6, 67.

This investigation was undertaken to prove whether the administration of dextroamphetamine with morphine would influence the analgesic action of morphine in human subjects. It is known that epinephrine has analgesic properties and that the analgesic action of morphine is enhanced in the dog and the mouse by dextroamphetamine; therefore it was hoped that with the combined administration of

morphine and dextroamphetamine it would be possible to relieve pain in man without producing considerable cerebral depression.

Twenty-one healthy medical students were used as subjects. 12 of whom served twice. Sixteen received 16 mgm. of morphine sulfate and 17 received a combination of 16 mgm. of morphine sulfate and 20 mgm. of dextroamphetamine sulfate. Pain threshold, blood pressure, pulse rate, choice reaction time, and flicker fusion frequency threshold were determined in each subject shortly before the injection and at thirty minute interval and two and one-half hours after the injection.

It was clear that dextroamphetamine enhanced the analgesic effect of morphine and at the same time tended to diminish and postpone side effects which might be undesirable such as nausea, vomiting, drowsiness and general depression. In determinations of choice reaction time both groups showed improvement. In the flicker fusion tests, however, the morphine produced a definite lowering of the flicker fusion frequency threshold which indicated less efficient performance at the same time. A slight rise in blood pressure was observed at the thirtieth and sixtieth minutes in almost all of the subjects given morphine, with a drop in pressure apparent only at the ninetieth minute. The combination produced a pronounced rise in the systolic blood pressure going as high as 35 mm. of mercury in 1 patient.

From all subjective and objective evidence it is clear that in normal subjects dextroamphetamine enhances, on the average, the analgesic action and decreases the cerebral depression due to morphine. It tends to counteract and possibly delay the onset of undesired side effects. It is believed that physicians may make use of the combination of drugs experimentally in selected cases. Dextroamphetamine should not be used in doses larger than 20 mgm. because of its effect on the blood pressure in some patients. Its use should be counteracted in patients with hypertension and delirium.

MARY KARP, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

McCort, J. J.: Roentgen Features of Chronic Tuberculous Peritonitis. *Arch Surg.*, 1944, 49, 91

Tuberculous peritonitis may be divided into two main types: acute and chronic. There are two varieties of the acute type: the military and the localized. In a small percentage of the localized type of peritonitis the tubercles break down and invade the greater part of the peritoneum and thus give rise to chronic peritonitis. Acute localized peritonitis is usually found in children. No roentgenological studies of this form have been reported.

Chronic tuberculous peritonitis is considered by pathologists to be a secondary infection in all cases. It may develop by one of three routes: (1) perforation, (2) lymphatic channels, and (3) blood stream. At the Massachusetts General Hospital, Boston, in the past five years 17 cases of tuberculous peritonitis were found among 182,390 admissions. In 3 the diagnosis was made on clinical grounds alone and in 14 on the basis of laboratory findings.

In the wet form of tuberculous peritonitis the plain roentgenogram taken in an early stage of the disease usually shows ascites with a low grade ileus. A diffuse haziness of the abdomen is seen with obliteration of the outline of the psoas muscles and the subperitoneal fat. The small intestine, which is usually filled with gas, appears to be floating freely in the abdomen. The diaphragm is elevated. In the dry form of tuberculous peritonitis the plain roentgenogram shows evidence of ileus alone. The small intestine is drawn up high in the abdomen. Examination of the colon by the barium-enema method is more informative. In tuberculous peritonitis the intestinal wall is rigid with areas of narrowing and areas of dilatation, and the bowel is freely movable in the peritoneal cavity. In roentgenograms taken after evacuation of the barium-sulfate enema, there is normally a descent of the entire transverse colon, but in tuberculous peritonitis there is little or no change in the position. Adhesive bands may be found retracting the intestinal wall.

Of greatest value is the study of the small bowel. The first abnormality noted is the rapid passage of barium, only about six minutes being required for transit. Rigidity and fixation of the loops of the small intestine are marked and there is little change in their position. The small intestine is shorter and occupies a smaller space than normal. In the intervening space the barium-filled loops of small bowel may be slightly widened and irregular because of the presence of fluid and fibrin between the peritoneal surfaces. The arrangement of the loops of the small bowel is irregular and bizarre. Abnormal segmentation of the barium-filled small bowel indicating a disturbance of the intestinal motility may also be distinguished.

The differential diagnosis is discussed. Six cases of tuberculous peritonitis are presented in 3 of which the preoperative diagnosis was suggested by the roentgen appearance of the large and small bowel.

HAROLD C. OCHSNER, M.D.

Ochsner, H. C.: Cholecystography with Beta (4-Hydroxy 3,5-Di Iodophenyl) Alpha Phenyl Propionic Acid. *Gastroenterology* 1944, 3, 23

The author gives a brief historical review of cholecystography beginning with February 1924, when Graham and Cole announced the revolutionary discovery of the use of calcium tetrabromphenolphthalein for intravenous cholecystography. The various contributions that followed have given rise to a voluminous literature. The drug that proved to possess the widest margin of safety was sodium tetraiodophenolphthalein which could be administered by the intravenous, or preferably the oral, route. This drug has been used almost exclusively since 1925.

In 1940 Dohrn and Diedrich reported their experimental work with another substance, the beta (4-hydroxy 3,5-di iodophenyl) alpha phenyl propionic acid which they called "biliselectan" but which in this country is known under the trade name of prodxal (Schering). Several articles appeared since then dealing with the clinical aspect of its use. All writers appear to have been impressed by the reliability of this new contrast medium and by the low incidence of toxic reactions.

The author himself has previously reported his favorable experience with 300 cases and now he extends his observations to 600 cases.

Since prodxal is largely excreted in the urine its only contraindication is serious renal disease, especially when there is retention of metabolites.

A single dose of 3 gm. is given taken in the form of 6 tablets each containing 0.5 gm. of the radiopaque substance. The author believes that the double dose in heavier patients is unnecessary. The procedure otherwise remains the same as with previous cholecystographic media.

In 56 per cent of the examined 600 patients, there was no reaction. In 5 per cent the reaction was mild and in 39 per cent it was somewhat more pronounced. Nausea occurred in 24.6 per cent (in a very few cases there was vomiting), diarrhea in 14 per cent, abdominal pain in 9 per cent and pain on urination in 5 per cent. In several cases there was an association of two or more symptoms.

The visualization of the gall bladder has been definitely superior to that obtained previously by the author when using the divided double dose of sodium tetraiodophenolphthalein. Confusing shadows in the intestine which were sometimes troublesome with the old dye were absent because of the predominant excretion of this new medium through the urinary tract.

A statistical compilation revealed that the visualization of the gall bladder was excellent or good in 67 per cent of the total cases, with presence of stones in 7 per cent and poor in 13.5 per cent, with stones in 47 per cent. In 18.5 per cent there was no visualization, with stones in 34 per cent of this group.

Slightly more than 10 per cent of the patients examined were operated upon. Surgical confirmation was satisfactory in all but 4 (6.3 per cent of the operative group). In these the gall bladder had been functioning normally, but evidence of cholecystitis was found by the pathologist.

The conclusion is reached that (1) proflax is a reliable cholecystographic medium which produces gall bladder shadows of excellent clarity, and (2) its administration is associated with fewer and less intense reactions than has occurred with sodium tetrastannophthalate. T. L. COTTELL, M.D.

McGee, J. J., Davidson, C. N., and Walton, H. J.: Determination of the Placental Site in Bleeding during the Last Trimester of Pregnancy. *Am J Roentg* 1944 42: 1.

Maternal mortality in placenta previa reported the literature from 1 to 10 per cent. Therefore it is readily understood why bleeding in the last trimester of pregnancy is a source of worry to the obstetrician.

An excellent historical review is given of placental visualization by means of roentgen rays. One of the first feasible clinical methods was demonstrated by Le Deum, and Lamer in 1934. They found that a diagnosis of placenta previa could be made on the finding of a soft tissue mass between the fetal head and the maternal bladder after the bladder had been filled with opaque media. The normal average distance between the fetal head and bladder was 1 cm. One drawback to the Ule *et al* method was that a definite diagnosis could not be made when the placenta was implanted on the posterior wall of the uterus with only a margin or a few centimeters overhanging the os.

In the same year (1934) that Ule *et al* made their studies, Snow and Powell demonstrated that the placenta could be visualized in a lateral view of the abdomen. No special apparatus or technical studies were necessary. All that is required is a soft tissue technique (300 ma.-sec. 36 in. distance and kilovolt to vary with the patient's thickness). Instead of the usual lateral abdominal technique, a bright light is used to visualize the placenta and the soft tissue of the abdomen. In addition, experience in the interpretation of such films is required.

A restudy of 132 cases at the University of Maryland Hospital from November 1938 to February 1943 was done. A correct diagnosis was made in 87.8 per cent. A correct negative diagnosis was made in 97 per cent of this group. A negative diagnosis is just as important as a positive one because the obstetrician can then allow the patient to go to term without worry of a sudden fatal hemorrhage. Marginal placenta previa was diagnosed correctly in 60 per

cent of the cases. In addition to diagnosing placenta previa, the obstetrician may be able to locate the position of the placenta, in the event that a cesarean section is indicated.

The technique used by the authors is described. An anteroposterior and lateral abdominal film is taken with 300 ma.-sec. 36 in. distance, Potter-Bucky diaphragm and from 65 to 75 kilovolts, the variation depending upon the thickness of the abdomen. The average thickness of the placenta is 6 cm.

The placenta was visualized in the majority of the cases by using the soft tissue technique. In doubtful cases a pneumocystogram was done. Air is preferred to opaque media for insertion into the bladder because it is cheaper, nonirritating and offers more contrast.

In placenta previa or low implantation of the placenta the vertical pelvic measurement is 2 cm., whereas the normal is 1.2 cm. An additional roentgen sign is the displacement of the bladder to either side when the placenta is on the lateral uterine wall.

The authors point out that roentgen examination for placenta previa does not eliminate the value and necessity of doing a sterile pelvic examination. Both examinations are complementary.

MATTHEW D. SUGGS, M.D.

Auerbach, O. and Stemmerman, M. G.: The Roentgen Interpretation of the Pathology in Pott Disease. *Am J Roentg* 1944 53: 57.

The classical roentgen signs of Pott disease are the narrowing of the intervertebral disc and the collapse of the vertebral bodies with or without the shadow of a cold abscess. During the past ten years the authors repeatedly found that these signs represent only part of the picture and that often the tuberculous involvement of the spine is considerably more extensive than could be suspected from the roentgen examination alone. The purpose of the present article is to try to co-ordinate these discrepancies.

The study is based on a material of 135 roentgen examinations performed at Sea View Hospital, Staten Island, New York, the presence of Pott disease being observed in 132 cases (9 per cent). Of the 132 patients, 100 had had roentgen examinations of the spine usually less than six months before death, so that a comparison of the pathological and roentgen findings could easily be accomplished.

The age distribution ranged between two and sixty-seven years, with 35 per cent of the patients being in the second and third decades of life. Fifty-five per cent were negroes, 43 per cent whites, and 2 per cent Chinese. Since at this institution the ratio of negroes to whites in the general autopsy material represented as 4 to 7, this preponderance of negroes appeared the more striking.

Of the 132 cases, 49 (37 per cent) were under 15 years of age, although the presence of the lesion was suspected in 18. There was an active chronic pulmonary process in only 35 (26 per cent) of the cases, a urogenital tuberculosis in 38 (29 per cent),

and both chronic and urogenital tuberculosis in 11 cases.

The number of vertebrae involved also varied. In only 6 of the 132 cases was there involvement of a single vertebra. In 39 (30 per cent) two adjacent vertebrae were affected, in 24 (18 per cent) three adjacent vertebrae, and in 63 (48 per cent) more than three. In the last group the disease was usually but not always found in contiguous vertebrae. The most severe case showed a contiguous extension from the fifth cervical vertebra to the coccyx. The lower dorsal and lumbar vertebrae were most frequently involved followed in order of incidence by the sacral lower cervical and upper cervical vertebrae.

From the pathological standpoint it is important that the affected bone may assume two forms: a productive (sclerotic) and an exudative (caseous destructive) form. If multiple vertebrae are involved the two forms may be found to occur in combination.

From the roentgen standpoint it is the destructive type of Pott's disease that acquires the well known classical appearance. When the vertebral body is collapsed and the intervertebral disc is destroyed the diagnosis is simple when the caseous process is limited to the central portion of the vertebra or its small parts, the diagnosis may be more difficult but the general clinical appearance of the patient and the demonstration of sinuses and fistulas etc. in the end will aid to clarify the situation. However in the essentially productive type of Pott's disease experience shows that a roentgen diagnosis is well-nigh impossible. In the authors series the destructive form of Pott's disease remained roentgenologically undiagnosed in only 10 per cent of the cases but the productive form was not recognized in a single instance, although at autopsy it was found in 25 per cent of all the examined cases.

In order to discover some signs that could be used roentgenologically to diagnose the productive type of Pott's disease, the authors made numerous roentgenograms of hemisections of spines taken at autopsy. They found under these roentgenologically ideal conditions, one change which occurred rather constantly. This change appeared in the form of "sclerosis," or an area of increased density corresponding exactly to the diseased areas noted grossly although pathologically these areas were nothing more than marrow spaces filled with granulation tissue and caseous material. In reviewing the roentgenograms taken before death with this change in mind, the authors were still unable to detect any thing of diagnostic significance. It is possible however that with a more specialized technique, and especially with serial roentgenograms, one may obtain better results. The demonstration of certain complications of Pott's disease may also assume, in this respect added importance. Such complications are the cold abscess which was noted in 96 per cent of the authors' cases at autopsy and the tuberculosis of the ribs which occurred in 18 per cent of the cases.

T. LEUCUTIA, M.D.

Pendergrass, E. P., Hodes, P. J., and Griffith, J. Q.: Effect of Roentgen Rays on the Minute Vessels of the Skin in Man. *Am. J. Roentg.* 1944 52: 123.

A preliminary study is reported on the immediate effect of roentgen rays on the minute vessels of the skin in man.

For this experimental study there were 84 white ambulatory patients. The extensor skin surface of each patient's midforearm was studied. Two areas of about 2 sq. cm., 4 inches apart, were marked off and studied. Precautions were taken to protect the forearm even against minor injury. A capillary count was taken in the morning after breakfast. One forearm was subjected to irradiation and the other was used as a control. Irradiation was given about one hour after the normal capillary count. A second and third capillary count was made six and twenty-four hours, respectively after irradiation. A final count was then made after a drop of histamine 1/1000 was injected near the area being studied.

Patients were divided into four groups according to the type of irradiation used. Technical factors used in the first three groups were almost alike: namely 200 kv., an oil immersed tube with equivalent inherent filtration of 0.25 mm. of copper 0.5 mm. of copper plus 2 mm. of aluminum filtration 20 ma., except in the third group in which 5 ma. were used. In the first group the target skin distance was 15 cm. with a 444 roentgen per minute output. Short tube skin distance was selected for high intensity. In the second group the skin target distance was 50 cm. with a 52 roentgen per minute output. In the third group at 50 cm. skin target distance and with 5 ma. the output was 10 roentgens per minute. For the fourth group a Chaoul contact therapy unit was used operating with 50 kv., 4 ma., 2 mm. of nickel inherent filtration and skin target distance of 3 cm. the output was 300 roentgens per minute.

The patients in all four groups were given irradiation amounting to from 300 to 333 roentgens per 2-sq.-cm. area at one sitting.

In Group I in which a short skin target distance was used (333 roentgens in three-quarters minute) the skin capillaries were dilated in six hours and after twenty-four hours most of them had disappeared. In Group II in which the skin target distance was 50 cm. (301 roentgens in seven and two-tenths minutes) the capillary dilatation was observed after six hours and to a lesser extent after twenty-four hours. In Group III in which the milliamperage was changed from 20 to 5 (308 roentgens in thirty and eight tenths minutes) no change was observed in the skin capillaries after six and twenty-four hours. In Group IV with a Chaoul contact therapy unit (300 roentgens in one minute) a moderate capillary effect was noted after six hours which became more marked after twenty-four hours.

Attention is directed to the differences in response of skin capillaries to irradiation. These differences are related to the method of irradiation.

MAURICE D. SACHS, M.D.

Mattick, W. L.: Some Experiences in the Treatment of Bronchial Cancer. *Am J Surg* 1944 52: 4

One of the greatest difficulties in treating bronchial cancer is our inability to make a sufficiently early diagnosis. Another is the tendency of every type of bronchogenic cancer to produce in a distant lymphatic permeation toward the hilar lymph nodes and a metastasizing hematogenous dissemination to distant parts of the body.

A review of 14 cases observed at the State Institute for the Study of Malignant Disease in Buffalo showed that approximately from 30 to 40 per cent of the patient had demonstrable metastases to the hilar nodes, egg nest lung bones, superficial nodes or liver when first seen. Operation then were poor risk for any therapy. There was left a group of between 10 and 15 per cent to whom aspiratory thoracotomy could be applied but in these too for one reason or another surgery was performed rarely. The most of the patient either because of necessity or desire on their part were referred for radiation therapy.

The latest best results have been obtained from 300-ky therapy although more recently 400-ky and even 1,000-ky therapy is being applied. The bronchial cancer is cross fired so as to build up a total dose of 2,000 roentgens with properly directed and angulated portals directed ventrally, anterior and two posteriorly. A supplementary course of similar irradiation after one or two months through previously nonirradiated portals probably three or four may be given.

In 4 selected cases gold radiation seed introduced through a bronchoscope may be implanted directly to the accessible cancer.

In 4 cases all proved histopathologically a long result ranging from three to five years were obtained. These cases are described in detail and illustrated with roentgenogram as well as with photographs of the histological section.

The conclusion is reached that such results while not entirely unusual, are better than indicated in many reports of the surgical radiation or combined treatment of this condition cited in the recent literature. T. LARSEN, M.D.

MISCELLANEOUS

Rntschler H. D. and Settle J. W. Jr. Treatment of Impaired Hearing by Radiation of Excessive Lymphoid Tissue in the Nasopharynx. *Penns Surg* 1944 72: 944-47-945

The literature indicates that there is a recurrence of the adenoid tissue in 75 per cent of the children having tonsillectomies and adenectomies before puberty. In many instances the orifices of the eustachian tubes are blocked by lymphoid tissue and hearing is impaired. Hearing impairment begins with the high tones and gradually involves the entire speech range. The earlier the treatment started for the defective hearing the better the results that can be obtained.

The authors believe that such conditions can be diagnosed early by routine school examinations in conjunction with the physician. In those instances where there is a massive recurrence of lymphoid tissue especially in the lateral walls of the pharynx, eustachian tube orifices, surgery is not particularly desirable. Lymphoid tissue irradiation by radium or radon or external irradiation may be used. Radium or radon is preferable inasmuch as the element can be placed next to the lesion which will minimize the amount of radiation given to normal tissue. Radium has the advantage over radon in that the tubes can be made long enough to fit the lesion, and the treatment time is shorter because a greater quantity of radon can be placed in each tube. A dose of 2 gm. in minutes to either side of the nasopharynx is sufficient. This may be repeated after a month, if necessary.

Internal irradiation has the advantage of being extracted and it is difficult to hold a child's head still. However, the mother properly protected, can hold the child's head. The irradiation that normal tissue receives is negligible. Treatment with 200-ky 1 mm. of copper plus 1 mm. of aluminum filters at 50 cm. focal skin distance and 100 roentgens to two lateral 6 by 8 cm. fields for four consecutive days usually sufficient.

Thirty-six patients received radiation therapy for impaired hearing associated with nasopharyngeal lymphoid hyperplasia. Sixteen patients were between the ages of seven and nineteen years and their hearing restored to normal and 7 had some improvement in their hearing. One patient, the history of mastoidectomy ten years previously and progressive deafness failed to respond to the treatment. The case histories are presented.

M. TUCKER D. SUGGS, M.D.

Simchowitz H. C.: German Radiotherapy in 1942 and 1943. *Br J J Radiol* 1944 17: 216.

The author, after a lapse of 10 years, has just received Volumes 2 and 73 (1942 and 1943) of *Strahlentherapie*. A reading of the published articles gives the impression that while British radiotherapy was advancing rapidly, German radiotherapy remained stagnant. Most of the articles are by German and Austrian authors with a sprinkling of Hungarians and Swiss. It is significant that there is no publication at all from the formerly leading German radiotherapy centers in Frankfurt (Hofmeister) or Hamburg (Hilthsen) and that Hoffelder has been invited by the German government to go as radiotherapist to Posen in occupied Poland, an honor which he apparently accepted.

Briefly some of the more important articles are as follows:

J. HENKEL (Heidelberg). Report of the Cancer Institute of the University of Heidelberg (on 5,000 cancer cases treated by radiotherapy alone). The five year cures which Simchowitz compares with those of the Christ Hospital and Holt Radium Institute of Manchester are as follows:

Heidelberg	Per cent	Manchester	Per cent
Total cures (of 5,000 cases)	8	Total cures (of 1,000 cases)	40
Breast (operable)	98	Skin	85
Skin	33	Lip	63
Lip	16	Floor of mouth	34
Floor of mouth	25	Cheek	29
Cheek	5	Tongue, anterior $\frac{1}{2}$	32
Tongue	7	Tongue, posterior $\frac{1}{4}$	1

K. G. ZIMMER (Berlin) Protective Material in Radium Work. Uranium, instead of lead or tungsten alloy is recommended.

A. KREBS (Frankfurt) The Total Radium Contents of the Human Body. The crematorium ashes of a great number of normal individuals (not of persons dying of radium poisoning) revealed an average radioactivity corresponding to $1.0-1.5 \times 10^{-4}$ gm. of radium element.

EWALD (Heidelberg) Radiotherapy in the Army. Irradiation of the spleen (100 roentgens) is recommended to promote coagulation of the blood pre or postoperatively in hemorrhagic diathesis.

H. BRAUNBERGENS (Freiburg) X-ray Therapy in Salivary Fistula. Since salivary fistula is not an infrequent war injury particularly in gunshot wounds temporary suppression of the parotid secretion is recommended by means of irradiation, which in most cases will produce a quick healing of the fistula. A dose of 300 roentgens given daily for from five to seven days is recommended. No permanent damage to the parotid gland has been observed up to the time of the report.

Other articles deal with the treatment of hemangioma especially in babies with Chaoul therapy or interstitial radium therapy also the treatment of spondylitis humeroscapular periarthritis Schueller Christian's disease of the skull, prostatic lesions carcinoma of the esophagus, carcinoma of the vulva and carcinoma of the larynx. Schink (Zurich) gives a very good review of recent advances in experimental cancer research and Zuppinger (Zurich) discusses the implications of the second course of protracted fractionated roentgen-ray therapy.

T. LUCUTIA, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Thomas H. B., and Lelphart, C. D. Septicemia and Purpura with Adrenal Hemorrhage in the Adult (Waterhouse-Friderichsen Syndrome); the Role of the Adrenal Gland in the Production of the Syndrome. *J. Am. Med. Ass.* 944 5 884.

The syndrome of bleeding into the skin and other organs including the adrenal glands, in the presence of a severe septicemia is becoming more frequently recognized by clinicians both here and abroad. Of 150 cases that have been reported previously, the vast majority occurred in infants and young children.

After some years of investigation by modern bacterial methods, it seems definitely established that the most frequently invading organism is the meningococcus. It is the growing opinion that the neisseria meningitidis will be indicted as the sole etiological agent. In the authors' review of 31 cases in adults, including 2 of their own, the meningococcus has been cultured or reasonably well identified on sections in 6 reports. The meningococcus is not universally accepted as the sole etiological factor. Lindsay and his associates reported 7 cases in children in which the heart's blood culture showed 4 to be positive to neisseria meningitidis, 2 to haemophilus influenzae and 1 to neisseria flava II. In case 2 of Sacks, the postmortem culture revealed a pneumococcus of type I. The occasional finding of the pneumococcus is of great interest because of its characteristic, like that of the meningococcus which produces purpuric skin lesions.

The concept that the hemorrhagic destructive lesion of the adrenal glands is the cause of the dramatic death of the victim has been accepted for a number of years. It is the opinion of the authors that death occurs from an overwhelming septicemia with a superinduced profound state of shock. The reason that massive adrenal hemorrhage excites interest is that it has long been known that loss of the adrenocortical hormone produces fatal disorders of systemic functions that are identical in most features with those of surgical or traumatic shock.

In the reported cases of recovery from the Waterhouse-Friderichsen syndrome the clinical features are identical with those that are fatal. It is difficult to visualize even mild bilateral hemorrhagic lesions of the cortex which could produce such profound disturbances in the individual and still allow recovery of complete function. The sequence of events in the production of the Waterhouse-Friderichsen syndrome is undoubtedly initiated by a bacterial invasion of the blood stream. That most cases of meningococcal meningitis show a stage of dissemination in the blood stream after a period of local infection in the upper respiratory tract is generally accepted. The cause of the wide hemorrhagic phenomena of

the skin, adrenal glands, and many other tissues has been thought to be the direct action of the bacteria or their toxins on the walls of the capillaries. Removal of the adrenal medulla will produce no definite change in the physiology of the animal, and it has been noted by many investigators that the surgical removal of both adrenal cortices will not produce the symptoms of insufficiency for at least several days. The clinical evidence for the concept that adrenal hemorrhage plays little or no part in the rapid death of the patient is furnished by Williams who states that adrenal hemorrhage is but an incident in an explosive disease that overwhelms all bodily resistance. The status of the thymolymphatic system plays no part in the adult cases. As the adult cases are similar to the juvenile, it may be assumed that it is almost never a factor.

The clinical picture is almost the same in adults as in children. The most common symptoms are malaise followed by chills, fever, sweating, and manifest weakness. General aching with abdominal pain or cramps and vomiting occur later. Cyanosis and the purpura are the symptoms which cause alarm. Laboratory examinations are frequently meager and inconclusive because of the short duration of the disease. Usually there is a rather accentuated leucocytosis. Chemical examination of the blood reveals the same findings that are generally found in shock. Rapid diagnosis can be made in smears of the purpuric areas.

The outstanding pathological feature is bilateral adrenal hemorrhage. Other postmortem findings are hemorrhage into the serosal cavities and intestinal tract, pulmonary engorgement and injection of the vessels of the brain and enlargement of the thymus, lymph nodes, Peyer's patches, and spleen. Two cases are presented in detail by the authors.

Therapy falls into two categories, specific and supportive. Chemotherapy with sulfadiazine in the form of the sodium salt should be given at once. About 0.05 gm. per pound of body weight is the initial dose to be given intravenously; the total daily requirement thereafter being approximately the same. The sulfadiazine level should be kept at 15 mgm. per 100 cc. Sulfathiazole is the drug of second choice followed by sulfapyridine and sulfanilamide. Polyvalent antimeningococcus serum should be started along with chemotherapy in doses of from 50 to 150 cc. intravenously, repeated every six to twelve hours for three doses, and daily thereafter if necessary. The intravenous use of meningococcus anti-toxin in 100,000 units may be substituted for the serum.

Supportive measures include the use of fluids and sodium chloride to combat dehydration, large and adequate doses of plasma to combat shock, oxygen, and the use of adrenocortical extract to combat the capillary permeability. Adrenocortical extract is

given twice daily in 10 cc. doses or the equivalent dose of the synthetic cortical derivative desoxycorticosterone. One dose of epinephrine may be given. The authors believe that early and less severe cases should be given all that modern therapeutics has to offer.

HERBERT F. THURSTON, M.D.

DUCTLESS GLANDS

Voitz, C. P., and Smull, K.: Hyperparathyroidism, with Failure to Recalcify after Removal of Parathyroid Adenoma. *Ann Int M* 1944 21 320.

A case is presented in which five years after the removal of an adenoma for the relief of hyperparathyroidism recalcification had failed to occur even though after the operation there was no evidence of recurrent hyperparathyroidism. Failure of bone recalcification despite the prolonged normal serum calcium level is attributed to the lack of increased osteoblastic activity which is suggested by normal preoperative and postoperative serum phosphatase levels.

WALTER H. NADLER, M.D.

Reveno, W. S.: Thyrotoxicosis Treated with Thiouracil. *J Am M* 1944 126 133.

The effect of thiouracil in the treatment of 9 ambulatory patients with toxic thyroid adenomas was studied for a period of eight months. In this series reactions in the form of urticaria, skin rashes, agranulocytosis, anemia, edema or jaundice were not observed. The time period before improvement became manifest from thiouracil therapy varied from two to fourteen weeks. Clinically 6 of the 9 patients showed significant improvement in thyrocardiac symptoms and a fall in the basal metabolic rate. Three patients failed to respond to thiouracil, one of these had received prolonged iodine medication. Histologically areas of hemorrhage and necrosis were found in the substance of the gland as a result of the thiouracil medication. It also appeared that iodine medication inhibited thiouracil hyperplasia of the thyroid.

BENJAMIN G. P. SHAPIROFF, M.D.

Moore, F. D., Sweeney D. N., Jr., Cope, O., Rawson, R. W., and Means, J. H.: The Use of Thiouracil in the Preparation of Patients with Hyperthyroidism for Thyroidectomy. *Ann Surg* 1944 120 152.

The ideal preparative drug for thyroidectomy would be one which so modified the underlying metabolic abnormality as to bring the patient to the surgeon with no evidence of thyrotoxicosis, this would allow him to remove the gland and produce permanent relief without subjecting the patient to the hazards of surgery while thyrotoxic. It was the purpose of the authors to ascertain to what degree thiouracil was given to 53 thyrotoxic patients as a preparation for thyroidectomy. Of these 34 have come to operation and have been followed up long enough to form a basis for study. Of these 34, 26 received thiouracil as the only preparative drug. The daily

dose was 0.6 gm usually administered as 0.2 gm in three doses. As a control series 35 thyroidectomies for thyrotoxicosis performed in the same hospital in the years 1941 and 1942 were selected the patients had been treated with iodine.

From their careful and well controlled work the authors found thiouracil superior to iodine because regardless of the degree of elevation of the metabolic rate prior to therapy it will bring the patient's basal metabolic rate to normal.

The histological change accompanying this lowering of the basal metabolic rate is an intensification of the hyperplasia seen in the thyrotoxicosis. Thiouracil produces a hyperplastic but nonfunctioning goiter. An occasional disadvantage of the use of thiouracil in preparing patients for surgery lies in the fact that this hyperplasia is accompanied by an increased vascularity and friability which makes the gland more difficult to handle and renders hemostasis arduous. The increased vascularity is especially troublesome if the patient has had a previous thyroidectomy.

Preliminary or concomitant iodine administration delays the thiouracil response. It is possible that iodine therapy subsequent to thiouracil treatment may play a useful role in reducing hyperplasia and vascularity.

Toxicity not unlike that of the sulfonamides may be expected to occur when patients are treated with thiouracil.

Thiouracil while an improvement over iodine as a means of preparing patients for surgery, is not yet the ideal drug for this purpose because it increases the histological abnormality of the disease. Also it affects only the production of hormone and not the underlying etiology of hyperthyroidism. Surgery may be rendered difficult because of the increased vascularity of the gland and lastly thiouracil is toxic to some of the patients.

EARL O. LATIMER, M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Warren, S., and Ehrenreich, T.: Multiple Primary Malignant Tumors and Susceptibility to Cancer. *Cancer Res.*, 1944 4 554.

In a series of 2,829 cancer autopsies 194 cases of multiple malignant neoplasms were encountered an incidence of 6.8 per cent. Together with the series previously reported there were 3,907 autopsies with an incidence of 6.0 per cent multiple cancers.

In the group of 194 patients with multiple malignant tumors there were 131 males and 63 females.

The average age of the male group was sixty-five and two-tenths years of the female group fifty-six and nine tenths years and of the entire group sixty-two and five tenths years.

The average duration from onset of the first tumor until death was two and seven tenths years.

The average interval between successive tumors when it could be determined was three and one tenth years.

Cases of multiple malignant growths occur more frequently than the expected incidence based on chance alone.

This greater frequency calculated as elevenfold may be attributed to susceptibility or predisposition to cancer in some persons or groups of persons.

JOHN J. MALONEY, M.D.

Haddow, A., Watkinson, J., Paterson, E., and Koller, P. C.: The Influence of Synthetic Estrogens on Advanced Malignant Disease. *Brit J J* 944 : 393

In the investigation of the mechanism of action of tumor producing compounds it was found that many carcinogenic hydrocarbons possess the property of retarding the growth of tissues, both normal and malignant. A few of the carcinogenic hydrocarbons possess slight estrogenic activity while in certain cases these two classes show interesting relationships on chemical grounds. Contrariwise, certain of the estrogens exert carcinogenic action in animals. The estrogens thus provide an example of compounds possessing growth-retarding properties and properties capable of producing a physiological stimulation of growth or the formation of tumors under certain circumstances.

The authors report the findings in 40 cases of carcinoma of the breast and in 33 cases of malignant disease in other organs treated with the synthetic estrogens triphenylchloroethylene triphenylmethylethylene or stilbestrol.

Of 23 cases of late malignant disease of the breast treated with triphenylchloroethylene 10 showed a significant although temporary retardation or even partial regression of the growth of the tumor. No evidence was obtained to suggest that the drug will prevent the development of metastases. The initial effect of treatment in these cases passes off comparatively rapidly.

Of 30 cases of advanced malignant disease other than cancer of the breast (including carcinomas of the skin, maxillary antrum, urinary bladder, ovary, rectum and testis, with reticuloendothelial growths and leucemia) similarly treated with triphenylchloroethylene, only 2 (carcinoma of the bladder and carcinoma of the prostate) showed undoubted partial regression of the tumor.

Of 4 cases of mammary cancer and 3 cases of Hodgkin's disease treated with triphenylmethylethylene (usually by intramuscular injection) only 1 (spheroidal-cell carcinoma of the breast) showed even a temporarily favorable response.

Of 14 cases of carcinoma of the breast treated with stilbestrol (by intramuscular injection or by mouth over a period of several months), 5 showed alterations in the growth and behavior of the tumor similar in nature to those produced by triphenylchloroethylene.

The cases reported afford no contribution to effective therapy but the results are of considerable fundamental interest, and provide an incentive to further investigation.

JOSEPH K. NARAT, M.D.

Gill, A. J.: Local Eosinophilia in Malignant Neoplasms. *J Lab Clin M* 944, 89-90

Eosinophile infiltration has been observed in many instances in the stromal tissues of a variety of neoplasms. It is most marked and is seen most frequently in cases of epidermoid carcinoma of the cervix. The neoplasm itself is not remarkable in appearance and there is no very impressive histological picture which distinguishes such tumors with the exception of the marked local eosinophilia which may be observed.

The inflammatory reaction in the stroma of carcinoma of the cervix is somewhat variable, although in most instances there is a rather marked infiltration of lymphocytes, plasma cells, and moderate number of large mononuclear cells. Polymorphonuclear eosinophiles occur with somewhat less frequency. Eosinophiles are present in the vast majority of cases, but usually are few in number and widely scattered. They are probably not much more numerous than might be expected in many chronic inflammatory processes. In a small percentage of cases these cells appear to be absent. However in another small group of carcinomas of the cervix there is an infiltration of eosinophiles which is definitely greater than that seen in the great majority and which in a few cases exceeds the number of all other inflammatory cells present.

The characteristic lesion of the type under consideration reveals a moderately undifferentiated epidermoid carcinoma, in the stroma of which there is a dense infiltration of typical eosinophiles. Occasionally the tumor stroma is entirely obscured by the large number of these cells which lie closely packed together.

The causes of the marked local infiltration of eosinophiles in some cases of malignant neoplasms are obscure. None of the usual explanations for eosinophilia seem entirely adequate. It is possible that special conditions of necrosis with liberation of protein-degeneration products, or unusual bacterial infection of ulcerated lesions, or perhaps a strong allergic susceptibility of an individual to either protein-degeneration products or bacteria may account for this phenomenon. It seems much more reasonable to assume that the reaction is due to some change probably degenerative in the tumor or in the tissue of the host, or in both. This may not be different from an allergic reaction of the host to a protein antigen.

What is thought to be a significant degree of local eosinophilia was observed in 77 per cent of a series of 309 cases of epidermoid carcinoma of the cervix. There is some reason to believe that the abundance of eosinophiles in the stroma of malignant tumors is of good prognostic import (other factors being equal), and probably represents a better than usual resistance to the advance of the neoplasm. It is hoped that future long term observations with follow-ups will confirm the value of this phenomenon as a favorable indication for the prognosis.

BENJAMIN GOLDMAN, M.D.

EXPERIMENTAL SURGERY

Price, P. B. Metcalf, W. Longmire, W. P. Hannon, C. R., and Rizzoli, H. V.: Experimental Shock. Effects of Acute Plasmapheresis in Healthy Dogs. *Bull. Johns Hopkins Hosp.* 1944 75 14

Whether or not shock produced by hemorrhage alone is similar to shock produced mainly by local fluid or plasma loss is a controversial question. In two series of experiments reported plasma and whole blood were removed under almost identical conditions; hence comparison seems valid.

After blood loss there is usually slight hemodilution after plasma loss there is a high degree of hemoconcentration. In both conditions, systemic anoxia finally occurs. In hemorrhage the mean arterial blood pressure is a fairly reliable index of shock, but the hematocrit is unreliable. In acute plasmapheresis the hematocrit is often the most dependable criterion. Vasoconstriction seems to be a less prominent factor in plasmapheresis than it is in hemorrhage. Cardiac output is much the same in plasmapheresis as in hemorrhage even though the blood is much more viscous. Hemorrhages into the adrenal glands are not so pronounced after plasmapheresis as they are after massive hemorrhage.

Uncomplicated posthemorrhagic death follows a fairly uniform pattern: the blood pressure declines slowly, breaks sharply, and death occurs from ten to twenty minutes later during the last two or three minutes the heart rate changes from rapid to slow and the respirations which were deep and fast suddenly falter before the heart stops beating. The course of acute plasmapheresis may be similar but in many cases, especially when the hematocrit is high, the heart stops suddenly the blood pressure, which may have been comfortably high, plummets to zero and the animal, after a few spasmodic respiratory efforts dies. Finally the postmortem appearance of the organs and tissues is somewhat different in the two conditions although in neither case is there much evidence of the "pooling" of blood extensive petechial hemorrhages or systematic capillary permeability.

Primary effects of acute plasma loss. These are hemodynamic: reduced blood volume, increased blood viscosity, decreased blood flow through the heart and body tissues, and low arterial and venous pressures. Fundamentally, these are simple physical effects, modified by physiological adaptations.

Secondary effects of acute plasma loss. If not compensated for, the vital functions of the blood are necessarily disturbed by the reduction of its volume by slowing of its rate of flow and by incomplete pulmonary oxygenation. A function of blood is to supply adequate amounts of oxygen to the tissues continuously particularly to vital centers and organs. Severe anoxemia quickly leads to dysfunction and death. Other vital processes such as the elimination of carbon dioxide, regulation of the body temperature, the water and electrolytic balances, nutrition and hormonal activities are likewise dependent upon

an efficient blood circulation. Consequently depression of the circulation by plasmapheresis might be expected to produce a variety of functional and organic abnormalities. Actually few were found in these acute experiments. The reason perhaps is that oxygenation is the function of the blood most promptly and seriously deranged by severe plasma loss and animals succumb from anoxia before other pathological changes have had time to become manifest. Furthermore the paucity of abnormal anatomical changes gross or microscopic, suggests that the deleterious effects of anoxia are largely functional.

The sudden failure of the circulation in late stages of plasmapheresis shock is not easy to explain satisfactorily. No abrupt vasodilation change of heart action, alteration in volume or concentration of blood, or abnormal capillary permeability was detected at the time of the break in the blood pressure. Some of the animals with high hematocrit and well sustained blood pressure collapsed rapidly and died without warning as though the heart exhausted by attempts to force viscous blood through the vascular system suddenly gave out entirely. There was no evidence of acute dilation of the heart.

The secondary pathological effects of acute plasmapheresis though vaguely manifested are of the utmost importance. They may be fatal. Anoxia resulting from an impaired circulation tends reciprocally to depress the circulation further and this vicious circle, if not broken, may lead to rapid collapse and death.

Replacement therapy is sometimes more successful in saving animals in the late stages of blood loss shock than animals in the late stages of plasma loss shock. This observation raises the question of whether irreversible changes are not more apt to occur in the latter condition.

Compensatory physiological adjustments. Small or moderate reductions of plasma volume do not usually produce the effects described because a number of physiological mechanisms are set in operation which compensate for such losses. It is only when the volume of plasma is seriously depleted that compensation fails and signs of shock develop.

1 The heart promptly begins to beat more forcefully and rapidly, tending to maintain a normal cardiac output and arterial blood pressure.

2 A degree of selective vasoconstriction occurs which shunts the blood from nonvital regions such as the skin through the more vital centers. This compensatory mechanism appears to be less effective in plasmapheresis than in hemorrhage because as has been mentioned vasoconstriction is probably less marked and the blood is much more viscous.

3 A small shift of fluid from the tissues increases the volume of plasma and tends to lessen hemoconcentration at the same time, activation of the red cell stores supplements the depleted blood volume but at the cost of hemoconcentration.

4 The coefficient of utilization of oxygen increases so that the hemoglobin gives up from 60 to 70 per cent of its load of oxygen instead of the usual

15 to 30 per cent. This adjustment is perhaps the most important and effective of these compensatory phenomena.

5. Hyperventilation increases progressively. It facilitates oxygenation of the pulmonary blood and aids in the elimination of carbon dioxide.

These compensatory mechanisms provide a wide margin of safety for normal individuals. That margin is narrowed by plasma loss. When the loss is large compensation eventually fails and anoxia develops. Whenever that happens spontaneous recovery is improbable.

Regeneration of plasma. After substantial but sublethal plasma losses in untreated animals water begins at once to be added to the circulating blood from twenty-four to forty-eight hours may be required for full restitution of the plasma volume. Replacement of the lost plasma proteins likewise starts promptly but progresses slowly. In one experiment, in which 26 per cent of the original plasma was removed and in which the dog was permitted to eat pellets and drink water *ad lib.* the absolute quantity of plasma proteins returned to the original value almost exactly forty-eight hours after the onset of plasmapheresis. When lethal amounts of plasma have been removed the relatively slow process of regeneration is interrupted in its early stages by death of the animal.

SMUEL KARM, M.D.

Hopps, H. C. The Role of Allergy in Delayed Healing and in the Disruption of Wounds. *Arch Surg* 1944 48 438.

It has been estimated that from 15 to 20 per cent of all wounds disrupt following abdominal operations. The disruption of wounds following operation may be due to (1) faulty surgical technique (2) inadequate closure of the wound (3) abdominal distention, coughing, or violent activity on the part of the patient, (4) infection of the wound (5) hypoproteinemia, (6) hypovitaminosis C and (7) constitutional states such as inanition, cachexia, severe anemia and jaundice.

The materials used as antigens in this study were (1) plain surgical catgut, (2) sheep intestine and (3) sheep serum.

Rabbits were used for the experimental studies. They were given varied amounts of material over extended periods of time.

It was brought out from this experimental study that hypersensitivity to catgut could be consistently produced in animals by sheep serum, catgut, or sheep intestine. Catgut stimulates the production of antibodies specific for itself in addition to antibodies which will react with either catgut or sheep serum. The antibodies specific for catgut may also be specific for collagen or mucoprotein. Heterophile antibodies do not react with catgut.

Experiments were carried out to evaluate the effects of hypersensitivity on the reaction of tissues to catgut sutures and on the healing of surgical wounds prepared with catgut. Rabbits were used in this study. Plain and chromicized catgut were used.

Routine sterile surgical technique was used throughout.

Experimentally there were 18 normal rabbits, 10 sensitized to sheep serum, 10 sensitized to sheep intestine, 16 sensitized to catgut, and 6 immunized against heterophile antigen. There was a very wide range in the titers. Biopsies were made at stated intervals. 142 biopsies were studied.

In the rabbits which were hypersensitive to catgut there was evidence of a slightly heightened reaction of the tissues to catgut sutures. There was no appreciable difference between normal rabbits and rabbits sensitized to catgut in the rate of dissolution or digestion of the catgut during the critical period of wound healing.

The healing laparotomy wounds prepared with catgut sutures showed no significant difference between those in normal rabbits and those in rabbits sensitized to catgut. The relative insolubility of catgut sutures is attributed to the absence of significant allergic reactions to catgut in wounds of animals sensitized to catgut.

The effect of local and anaphylactic reaction within the tissues of a healing wound were investigated. Rabbits which were sensitized to either horse serum or egg albumin were used. Abdominal operations were done in the experiment.

Among 37 rabbits with laparotomy wounds, 11 had been sensitized to horse serum and 15 to crystal line egg albumin. Six controls were used. Twenty-five of the 31 sensitized animals received a specific antigen intravenously after operation. Twelve of the sensitized rabbits receiving specific antigen died of anaphylactic shock.

There was no significant difference between the two groups of animals in the reaction to the suture, in the state of the sutures, in the degree of general inflammatory reaction in the plane of incision, or in the amount of edema in the intact tissue.

Microscopically the ratio of macrophages to fibroblasts was considerably greater in animals which had received specific antigen after operation. The biopsy specimens in this group did not show a single fibroblast although macrophages were plentiful nine days postoperatively. In this group the reticulum was finer and there was less collagen than was found in the control animals. The tubing fluid in which the catgut is immersed is quite potent as an inflammatory agent and may produce an Auer reaction.

In normal as well as in sensitized control animals which have received nonspecific foreign proteins, wounds heal without significant untoward reaction. Apparently the most obvious explanation is that a local anaphylactic reaction plays a predominant part. This is a direct or an indirect effect of general anaphylaxis and the local formation of antibodies.

As a precautionary measure, when abdominal operations are performed in the presence of chronic abdominal inflammatory lesions in which such a reaction may occur the abdominal wounds should be thoroughly re-enforced with nonabsorbable sutures.

ROSE and J. BROWN, J. M.D.

Waud R A: The Absorption of Sulfathiazole from Wounds. *Canad Jt Ass J* 1944 51 239

Estimations of the concentration of sulfathiazole at different levels below the floor of wounds have been made at stated periods following the application of different concentrations of the drug and when the latter was incorporated in different bases.

The higher the percentage of the drug in the base the greater was the concentration obtained in the tissues.

The concentration obtained in the tissues beyond 2 to 3 mm. below the surface of the wound is much less than that ordinarily reached when sulfathiazole is given by mouth. This may not be sufficient to prevent the spread of infection and may justify the systemic administration of the drug.

The level of sulfathiazole obtained in the blood when the drug is applied locally approximates that of the tissues situated at a level anywhere between 3 to 7 mm. below the surface of the wound.

The delivery of sulfathiazole out of a water soluble base or an oil in water emulsion takes place quite readily. When incorporated in a fatty or paraffin base and applied to an open wound very little of the drug reaches the tissues. When suspended in a liquid oil the sulfonamide falls out and is deposited in almost pure state on the surface of the wound or dressing.

HOWARD A. MCKNIGHT, M.D.

Brunschwig, A. and Thornton, T. F., Jr.: An Experimental Study of the Lateral Spread of Epidermoid (Squamous Cell) Carcinoma in Man, and the Reaction of Such a Lesion to the Wound Healing Stimulus. *Cancer Res* 1944 4 515

Previous experimental studies in mice and histological studies of specimens from human beings were interpreted to suggest that squamous-cell carcinoma arises by malignant transformation of a segment of squamous epithelium, and not as a result of such changes occurring in one cell or a small nidus of cells. The experimental evidence also was interpreted to indicate that while the principal factor in the increase in size of such lesions was the increased number of cells resulting from continuous mitotic activity, progressive malignant change in the normal epithelium immediately apposed to the malignant epithelium also contributed to lateral spread of the process. This hypothesis admittedly has few adherents today.

Another observation made on mice bearing methylcholanthrene squamous-cell cutaneous carcinoma was that when the carcinoma was bisected and one half of it removed and normal skin was then approximated to the cut edge of the growth by suture with subsequent spontaneous separation of the wound to produce a chronic ulcer, healing of the latter was attempted by epithelial growth from the side of the normal epithelium and not from the margin composed of malignant cells. However the neoplasm did increase in size in the direction away from the cut

edge that is lateral spread took place over the continuously intact margins of the growth.

In a patient presenting a squamous cell carcinoma of the left hand the lesion was bisected and one half was removed together with a semicircular patch of skin. A fresh wound was thus created, one margin of which was composed of malignant epithelium. The course of events in this patient closely paralleled the observations reported in similar experiments with cutaneous squamous-cell carcinoma produced by methylcholanthrene in mice. The wound healing stimulus obtained by the surgical excision of tissue did not locally stimulate the growth of the neoplasm. Indeed the malignant squamous epithelium appeared strikingly indolent toward such a stimulus, and seemed to have lost the property of purposeful proliferation to cover denuded areas. On the other hand, growth was progressive in areas which were undisturbed and the histological findings here were consistent with the hypothesis of progressive cancerization of normal cells as a factor in the lateral spread of squamous-cell carcinomas. The intactness of the original junction zone between malignant and non-malignant squamous epithelium appeared to be a factor contributing to the lateral spread of this type of malignant process.

SAMUEL KAZIN, M.D.

HOSPITALS MEDICAL EDUCATION AND HISTORY

Lemon H M, Wise H, and Hamburger M Jr: Bacterial Content of Air in Army Barracks: Results of a Study with Especial Reference to the Dispersal of Bacteria by the Air Circulation System. *Am J Med Chic* 1944 6 91

The epidemiological problems which arise in war time as a result of crowding together of large populations in semi-isolated communities are well recognized. The spread of acute infections whose portal of entry is the respiratory tract is particularly enhanced by prolonged close association of large numbers of persons. Although some excellent investigations have been made concerning the influence of various immunological and environmental factors on the incidence of certain forms of air-borne disease in military and civilian populations, little is as yet known concerning the exact mechanism involved in the actual transfer of respiratory disease agents from man to man. While this transfer may in part be accomplished by a direct aerial dissemination of micro-organisms in fine droplets scattered by a sneeze or cough, it has become apparent that there are important secondary reservoirs for respiratory pathogens especially in bedding, clothing and floor dust.

While the major source of the large numbers of air-borne bacteria found in such environments as army barracks is not known, it seems likely that secretions expelled from the human nasopharynx contribute substantially to this heterogeneous bacterial population and certainly constitute the primary source of air contamination with respiratory patho-

gens. This study provides considerable evidence that floor dust, bedclothes, and probably the soldiers' clothing provide a major secondary reservoir of air-borne micro-organisms. Recent studies in wards housing patients with hemolytic streptococcus infections of the throat showed that changes in the number of hemolytic streptococci recoverable from the air paralleled variations in the total bacterial count.

Air entering the room from the delivery ducts is usually considerably lower in bacterial content than adjacent room air at either upper or lower bed levels and dilutes to a greater or lesser degree the concentration of bacteria in the room air. When one considers the enormous increase in air-borne bacteria which occurs each day as a result of the usual routine of dressing, making beds, and the dry sweeping of floors, it becomes apparent that in general the danger of air-borne infection to the soldier population is greater from this local initial pollution of air than from redistribution of disease agents through the air circulation system.

While complete control of the secondary reservoir may not be possible it would seem reasonable to assume that much could be done to diminish the dispersion of bacterial particles, especially from the floor and bedding. Some progress in this direction has already been made. The difference in dust raising between moist and dry floor sweeping is too well

known to require emphasis, but there is less appreciation of the possibilities for dissemination of dust and bacteria from infrequently cleaned blankets.

The concentration of air-borne bacteria in some barracks was found to depend on the number of men present at any one time and on the amount and type of their activity. Even when men had been asleep for several hours there were more bacteria in the air than when the barracks had been vacant for a similar period. The largest number of bacteria was found during the greatest activity of the men, e.g., at times of dressing, bed making, and dry sweeping of the floor.

Group A beta hemolytic streptococci were isolated in small numbers from only 3 per cent of the air samples. In 1 instance a large number of group B type 3 streptococci were recovered near a contaminated bed during bed making. Although the air circulation system was shown to disperse bacteria throughout the barracks under normal conditions of operation it would seem to afford a smaller hazard for spread of air-borne infection than is offered by contaminated dust raised during activities of the men themselves. Studies of this nature provide a new approach to investigation of the spread of acute diseases of the respiratory tract and may serve as means of evaluating special measures employed to reduce air contamination in dwelling places.

JOHN E. KILPATRICK, M.D.

February, 1945

International Abstract of Surgery

*Supplementary to
Surgery, Gynecology and Obstetrics*

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INTERNATIONAL ABSTRACT OF SURGERY

VOLUME 80

FEBRUARY, 1945

NUMBER 2

ABSTRACTS OF CURRENT LITERATURE SURGERY OF THE HEAD AND NECK

EYE

Lancaster W. B.: The Present Status of Eye Exercises for Improvement of Visual Function
Arch. Ophth. Chic., 1944, 32: 167

There is abundant evidence for the general proposition that exercises repetition practice and learning lead to better performance and to the acquisition of skill. Many ocular conditions exemplify this law. Since seeing is only partly a matter of the image on the retina and the sensation it produces and in still a larger part a matter of the cerebral processes of synthesis in which memories play a principal role, it follows that by practice by repetition, and by exercises one builds up a substratum of memories useful for the interpretation of sensations and facilitates the synthesis which are the major part of seeing. Also motor functions are perfected by practice and by learning and reflex pathways are facilitated.

Ophthalmologists have neglected this field, leaving it to irregular half-trained workers while they have concentrated their attention on the primary source of the sensation, the image on the retina.

The author is convinced that there are valuable possibilities in this field awaiting intelligent development. He is skeptical however regarding structural changes which are wrought by exercises other than hyperplasia and hypertrophy of the muscles and the consequent changes induced in the tendons, and perhaps in the bones.

EMIL C. ROSENBERG, M.D.

Brown A. M.: Prostheses for the Eye and Orbit.
Arch. Ophth. Chic., 1944, 32: 308

Two overcorrections are necessary in making a prosthetic eye and lids. The entire orbit should be sculptured slightly higher on the face than it appears on the other side and the conjunctiva should be



Fig. 1. Face after surgical extirpation of the entire orbital contents for retino blastoma. A without, and B with, a prosthesis. The prosthesis had to be designed as a relatively thin sculptured patch to avoid contact with the exposed sinuses.

slightly more viable in the prosthesis than in the normal eye

In this article Brown describes in detail a method which has proved satisfactory in his work but which can be variously modified to meet individual requirements

ERIC C. ROBINSON, M.D.

EAR

Quayle, A. F.: Otitis Externa in New Guinea. *Med J Australia*, 1944, 2: 8.

Quayle states that the incidence of otitis externa in Australian troops in New Guinea is discussed.

The most prevalent type desquamative otitis externa, is described.

It is considered unlikely that the condition is caused by a fungus. Bacteriological examination suggests that it is actually an infection of the skin of the ear canal with *Pseudomonas pyocyaneus* or coliform bacilli. It is seen only rarely in natives.

Treatment is considered, the essentials being the complete removal of desquamated epithelium, and the reduction of swelling by packing

JAMES C. BRASWELL, M.D.

Collins, E. G., and Hughes, K. E. A.: The Treatment of Chronic Suppurative Otitis Media by the Local Application of Penicillin and Other Drugs. *J. Laryngol.*, 1944, 59: 81.

In contrast to acute suppurative otitis media in which penicillin-sensitive organisms are frequent, the initial cultures in chronic otitis media showed the staphylococcus in only 3 ears whereas a coliform bacillus was found in 10 the proteus was found in 13 and diphtheroids in 6 of a total of 26 ears. Cultures were mixed in some instances. Cultures were made by means of a platinum loop introduced into the middle ear through the perforation. These organisms are considered to be not only saprophytes but they are of etiological significance in the persistence of the discharge

Nine patients were treated by the local application of penicillin. After cleansing by intratympanic syringing penicillin was forced into the middle ear by a Politzer bag and then applied at eight hour intervals on a wick leading into the middle ear. Two cases were treated by irrigations following mastoid surgery. Under treatment subsequent cultures showed a frequent contamination of the middle ear by the staphylococcus. Disappearance of the penicillin-sensitive organisms occurred routinely in about five days but recurrence of the staphylococci usually occurred later. Conclusions were that the use of penicillin was disappointing in the treatment of chronic middle-ear suppuration. It has no curative effect on the coliform or proteus bacilli and in cases of the former type an acute otitis externa frequently occurred. In penicillin-sensitive infections the value of the drug is limited because of the mechanical problem of getting contact with the diseased area. Also success cannot be expected in extensive mastoid disease or cholesteatoma.

The use of boric acid in 75 per cent alcohol is found to have a good effect in one-half of the patients with a coliform-bacillus infection. Neither the proteus bacillus nor the staphylococcus and streptococcus appeared to be influenced to any extent. Boric iodine powder gave similar results, although it was more effective in the coliform infections. In both cases the drying effect was considered of primary importance. Several preparations of sodium molybdate were used locally. Of these the molybdate sulfathiazole seemed most suited for application. None of these preparations appeared to influence the proteus cases but some effect was obtained on the coliform cases. The staphylococcus and the proteus bacillus proved in general to be the most intractable to treatment. Other factors such as nasopharyngeal sepsis, the presence of granulomas, and chronicity may have predisposed to failure. The external route of infection of the middle ear in such cases is important and protection against reinfection while healing should be insured.

JOHN R. LINDSEY, M.D.

Atkinson, M.: Ménière Syndrome; Results of Treatment with Nicotinic Acid in the Vasoconstrictor Group. *Arch. Otolaryngol.*, 1944, 49: 201.

Atkinson finds that in cases of idiopathic Ménière syndrome one of two vascular mechanisms is at work, a primary vasodilator and a primary vasoconstrictor mechanism, either of which can produce the characteristic picture. These two groups can be differentiated by means of an intradermal test with histamine. The treatment appropriate to one group is inappropriate and deleterious in the other and therefore accurate grouping is a prime requisite for effective therapy.

Elsewhere the author has published satisfactory results obtained by desensitization in the primary vasodilator group. This article is concerned with the method and the results of treatment in the primary vasoconstrictor group that much larger group in which the response to histamine injected intradermally is normal.

It is believed that in cases of Ménière's syndrome belonging to the primary vasoconstrictor group the disturbance is due to anorexia of the labyrinth caused by vasospasm and that the treatment therefore logically calls for a vasodilator drug. In a series of 110 cases the patients were treated medically exclusively with nicotinic acid by a method described in this report. The attacks of vertigo were relieved or greatly modified in 84 per cent of the cases.

NOAH D. FARRINGTON, M.D.

NOSE AND SINUSES

Colbert, R. M.: Osteomyelitis of the Frontal Bone Treated with Penicillin. *A. N. Otolaryngol.*, 1944, 53: 5.

The use of penicillin in osteomyelitis of the frontal bone gives promise to preclude the radical surgical procedures ordinarily employed, with their attendant deformities.

Penicillin alone cannot be depended upon unless drainage is established surgically. Therefore penicillin definitely has its limitations and must be used as a supplementary measure to surgery or vice versa.

Drainage stops fairly rapidly after primary evacuation of the pus when penicillin therapy is instituted. Constant or frequent local penicillin application is essential even after cessation of the parenteral injections.

At least two weeks of serial sterile cultures of a wound should be obtained before it is allowed to close.

The fact that penicillin has overcome the acute infections caused by staphylococci and the sulfonamide-resistant streptococci indicates that penicillin is an exceptionally potent antibacterial agent.

JOHN F. DEXLER M.D.

PHARYNX

Marino, H. Total Pharyngoplasty (Faringoplastia total). *Prensa Med Argent* 1944 31 1509

Plastic reconstruction of the pharynx is rarely necessary as it is required only after the extirpation of tumors involving the larynx and pharynx. It may be performed at the time of the operation for tumor or at a later date. Generally the latter time is preferred as the patients usually cannot bear the additional operation after removal of the tumor. However the surgeon who performs the first operation should take into account the possibility of the later plastic operation so as to leave the orifices in as favorable a condition as possible and preserve the skin necessary for the flaps.

Two forms of the operation are described and the steps illustrated. In the first, incisions are made at equal distances from the midline and running from the chin down to the esophagotomy opening. The skin flaps are dissected free on each side and united and sutured in the midline and the ends of the tube are sutured into the opening in the floor of the mouth and into the esophagotomy opening. The loose skin is brought over from the sides and sutured over the wound. In the second the incision on one side is made from 6 to 7 cm. from the midline and on the other 3 cm. from the midline. The broader side is dissected free, brought over to the incision on the other side and sutured to it to form the tube. A cervicothoracic skin flap is brought down to cover the bleeding surface and skin grafts are used to cover the two narrow remaining bleeding surfaces.

Two cases in which this operation was performed are described and illustrated with photographs of the patients. In the first case the first type of operation was performed for epithelioma on January 20 1944. The new formed pharynx functioned well up to July 14 1944 when two fistulous tracts opened in it and relatively severe hemorrhage took place. The patient's general condition indicated recurrence of the tumor.

The second operation was also performed for epithelioma of the larynx. Six weeks after removal

of the tumor pharyngoplasty was performed by the first technique. After some time a pulmonary complication developed and the sutures broke down. The plastic operation was repeated by the second technique and at first the neopharynx functioned well. After a time however the patient had difficulty in swallowing and roentgen examination showed a tumor mass evidently cancerous at the cardia. Within a week he died of copious hemorrhage from this tumor. AUDREY G. MORROW M.D.

NECK

Woodson B.: What Can We Do for Myasthenia Laryngis? *Ann Otol Rhinol*, 1944, 53 502

Myasthenia laryngis is a name applied to a morbid entity characterized by asthenia of the phonatory musculature of the larynx, especially the powerful overworked thyroarytenoid muscles.

Constant, excessive use of a very high or a very low pitch is the primary cause for myasthenia laryngis.

Given a complaint of recurrent hoarseness, tired voice and loss of tone with a mirror view of the larynx showing an elliptic chink in the vocal cords we can make a diagnosis of myasthenia laryngis provided we have eliminated other causes.

Prophylaxis is the essence of the successful treatment as a cure can be obtained only in the early stages of the disease. The author has had no beneficial effects from the use of prostigmine.

Relaxation of the muscles of phonation by special exercises is of great value for preventing a recurrence but prolonged absolute silence and rest must always precede any treatment.

The middle register must be used to the exclusion of constant very high or very low pitches in singing or in talking.

JOHN F. DEXLER M.D.

Ferguson G. B.: Hemangioma of the Adult and of the Infant Larynx: A Review of the Literature and a Report of 2 Cases. *Arch Otolaryngol* Chic. 1944, 40 189.

To date, 123 instances of hemangioma of the larynx have been recorded in the available literature. Two distinct classes have been described: the adult cases (116) and the infantile cases (7). One additional case in each class reported herein makes the total 125 cases.

In several instances the diagnosis of hemangioma of the infantile larynx was not made until postmortem examination. However dermal hemangioma, a lesion associated with recurring afebrile laryngeal obstruction may suggest the proper diagnosis of this form of laryngeal hemangioma.

The opinion of the majority holds tracheotomy to be the most suitable method of relieving dyspnea caused by hemangioma of the infantile larynx. Small tumors of the adult type of hemangioma may be removed by forceps. Larger tumors demand a careful selection of approach, which may be made through the mouth, by laryngofissure or by lateral pharynx

gotomy Electrodesiccation, surgical excision, or irradiation may be successful. J M. MORA, M.D

Montserrat, J. L.: Epithelioma of the Larynx (Epithelioma de la laringe) *Rev As med. argent* 1944, 58 670

This is a statistical review of the subject of epithelioma of the larynx, illustrated with graphs, tables and photomicrographs of the histological findings in a number of the cases. The author made a study of 350 cases of tumors of the larynx 180 of them from biopsy material 42 from autopsies, 13 from museum pieces and 15 from operative material. Among the 198 cases in which the sex was given 190 were men (95.95 per cent) and 8 women (4.05 per cent). Among the 197 cases in which the age was given the youngest patient was twenty three years of age and the oldest eighty 36.55 per cent of the patients were between fifty and fifty-nine years of age 30.46 per cent between forty and forty-nine and 15.73 per cent between sixty and sixty-nine.

Among 10,830 autopsies in the Instituto Telémaco Suximi there were 3,021 cases of cancer of which 42 were in the larynx therefore cancers of the larynx were found in 0.38 per cent of the total number of autopsies and in 2.1 per cent of the total number of cancers. Among 543 cases in which histological examinations were made 82.3 per cent were prickly-cell epitheliomas divided into sub-varieties depending on the degree of differentiation and atypia 3.7 per cent were epidermoid 16.45 per cent had horny pearls, 2.87 per cent were dyskeratotic, 44.03 per cent were moderately differentiated and 15.22 per cent were only slightly differentiated.

Intermediate pavement epitheliomas constituted 5.34 per cent basal-celled 1.23 per cent and finally atypical cases 10.18 per cent.

Topographically they were divided into pure laryngeal tumors laryngopharyngeal tumors, and laryngoglottic tumors. The first group were divided into supraglottic, glottic, infraglottic, and generalized. Of the total, 69.5 per cent were supraglottic and were divided into epiglottic (42.75 per cent) cord-ventricular (18.14 per cent) and aryepiglottidean fold (8.24 per cent). The glottic tumors made up 26.3 per cent of the total and included those of the vocal cords (18.55 per cent), and those of Morgagni's ventricular cavity. The infraglottic tumors made up 2.3 per cent of the whole, and the generalized forms 2 per cent.

AUGUST G. MORAN, M.D

Howes, W. E., and Plateau, M.: Carcinoma of the Larynx: A Review of Treatment and End-Results at the Brooklyn Cancer Institute. *Arch. Otolaryng. Chic.*, 1944, 40 133

Only carcinoma arising on the vocal cords (intrinsic) was observed to be amenable to surgical treatment in this series of cases. Radiation therapy was shown to be of value in the treatment of both carcinoma arising on the cords and carcinoma of the extrinsic structures of the larynx. Of 68 men and 3 women with lesions proved to be carcinoma of the larynx, who were admitted to the Brooklyn Cancer Institute from 1934 through 1943 17 are living. Of the surviving patients, 12 had carcinoma originating in the intrinsic larynx, and 4 in the extrinsic larynx.

NOAH D. FARRINGTON, M.D

SURGERY OF THE NERVOUS SYSTEM

PERIPHERAL NERVES

Elkington J St. C. Prognosis of Peripheral Nerve Injuries. *Proc R Soc M, Lond* 1944 37 547

The prognosis with regard to recovery in peripheral-nerve injuries is discussed relative to the individual nerves

The radial nerve has been found to regenerate more rapidly and completely than any other peripheral nerve. While recovery may not be complete, very useful function of the involved muscles returns in a good percentage of cases

The ulnar nerve is considered the most disappointing and unsatisfactory from the standpoint of recovery of function following injury and repair. Although a fair degree of function may return in the long flexors supplied by the ulnar nerve there is often little or no recovery in the hand muscles

The median nerve shows a recovery level between the radial and ulnar nerves. Here again, recovery in the long muscles of the forearm is much better than recovery in the small hand muscles supplied by the median nerve, which, as a rule is incomplete and functionally unsatisfactory. Fair degrees of recovery in the sensory mechanism of the median nerve results in a good percentage of cases particularly in injuries nearer the wrist.

The sciatic trunk, in the author's experience has not shown the degree of recovery one might expect following what appears to be a satisfactory anastomosis. Recovery in the gastrocnemius and soleus and tibialis posterior muscles is fairly good but muscles of the anterior tibial group are rather disappointing and recovery in these is not frequently seen. Sensory recovery has resulted in rather crude sensation to pinprick and temperature over the sciatic distribution. The mechanism of the foot is usually seriously affected as a result of the incomplete recovery in muscular function.

The peroneal nerve has recovered poorly from the motor standpoint on the whole despite a fair recovery of sensation. The tibial nerve shows a return of crude sensibility in the sole muscular recovery seldom proceeds beyond the proximal muscles of the calf

The author concludes from these observations that the smaller the muscle and the more delicate its function, the less likely it is to make a satisfactory functional recovery after a period of denervation.

The factors modifying the average prognosis in common peripheral-nerve injuries are

1. Wounds which are complicated by heavily infected compound fractures and severe destruction of the soft tissues as well as considerable loss of continuity of the nerve.

2. Date of suture this factor may be complicated by infection and it is suggested that the minimum of three months be allowed to elapse between com-

plete healing of the wound and an attempt to suture the nerve

3. Individual factors There is some reason to believe that nerve regeneration (as with any other process of healing) may vary in different individuals. The only factor here considered was that of age and the observations would indicate that the younger the patient, the better the outlook as far as nerve recovery is concerned

Recovery of function in the part enervated by the nerve is stressed. The preservation of the most complete possible degree of mobility of every part of the limb affected is important in preserving the maximum of ultimate function. Excess splinting often results in unnecessary joint stiffness and considerable functional loss. Psychotherapy and occupational therapy are also of importance in effecting the maximum degree of rehabilitation

Rehabilitation for Army service in the British Army has been low in patients who have had peripheral nerve injuries sufficiently severe to require exploration. Apparently over 10 per cent of the enlisted men in this group could be returned to some type of Army service in a lower category

HOWARD A. BROWN M.D

Learmonth J R.: Personal Experience of Exploration and Re-Exploration of Injured Nerves. *Proc R Soc M Lond* 1944 37 553

The author has set down certain indications for exploring an injured nerve irrespective of the clinical findings. These may be listed as follows (1) previous long-continued sepsis in the wound (2) a nerve lying at the bottom of a healed trough wound (3) a history of an unusually severe bleeding from a muscle mass (4) enclosed crushing types of injury (5) a nerve or nerves and the main artery to an extremity having been injured at the same level (6) two or more nerves of the same limb having been injured and (7) persistent pain or persistent hyperhidrosis in the cutaneous distribution of the injured nerve.

Decision for or against excision and suture in cases of partial division is often difficult. It is advised that these be let alone when there is a fair degree of motor or sensory function in the median or ulnar nerve groups.

Skin grafting over the areas (either split graft or full thickness graft) should precede operative repair of the involved nerve

Conservative treatment is advised when there has been gross loss of tendon and muscle tissue and it is obvious that useful movements cannot be restored

Re-exploration of a nerve previously operated upon depends upon the interval which has elapsed since suture, the level of the lesion, and the absence of any evidence of nerve recovery after an adequate time has elapsed. Postganglionic sympathectomy

has been tried in a number of cases in an attempt to decrease the total number of axons competing for the tubes in the distal segment following end-to-end anastomosis. No estimate of results is given at this time.

HOWARD A. BROWN, M.D.

Botterell, E. H., Keith, W. S. and Stewart, O. W.: Results of Surgical Treatment of Sciatica Due to Herniation of an Intervertebral Disc in Canadian Soldiers Overseas. *Canad. M. Ass. J.* 1944, 51: 20.

The authors report the results of a follow up study on 51 cases of herniated nucleus pulposus in which an attempt was made to ascertain the outcome of operation on the patients. The personnel, however, was entirely that of the Canadian Army and military cases do not react the same as those in civil life. It is emphasized that careful selection of the cases for operation is extremely important, and that it is quite impossible to operate in every case in which the symptoms appear. In the majority of the cases, conservative treatment was administered for a period of three weeks, and the patients were observed for any improvement under this type of management. In some of the cases the diagnosis was supported by pantopaque or oxygen myelograms. Operation was never done on patients who appeared to be emotionally unstable, or who had some physical defect. It was found very important to ascertain whether or not the patient was desirous of carrying on in the Army and in the event that he did not wish to do so operation was not performed. The operative procedure is said to have been the same as that carried out by neurological surgeons.

Postoperative care consisted in keeping the patient in bed for two or three weeks and reconditioning was commenced during the last few days in bed in the form of tension exercises. A few days later restrictive physical exercises were started and the range of movement was increased gradually until the patient was able to carry on in the back class. The entire procedure was carried out under the supervision of the surgeons.

The article is accompanied by tables which show the breakdown of the patients who were investigated.

There were approximately 100 men in the original group. All of the 51 patients who form the basis of this study had an operative diagnosis of herniation of a lumbar intervertebral disc. Twenty nine men were returned to full duty, 14 were returned to sedentary duty and 8 were unfit for military duty.

ARTHUR VERNSTROMER, M.D.

De Rezende, N.: Nerve Grafts from Cadavers in Human Surgery (*Enxerto de nervos do cadáveres em cirurgia humana*). *Rev. brasil. cir.* 1944, 3: 7.

The author discusses the use of nerve grafts from cadavers in the repair of nerve injuries. Nerve grafts have been used chiefly in military surgery. The graft must be taken from the cadaver not more than twenty four hours after death. The technique of taking the graft and of fitting it into the nerve to be

treated is described. The author uses a 50 per cent solution of gum acacia to cement the graft into the lacerated nerve. After the operation the patient is given subcutaneous or intramuscular injections of cholinergic drugs such as vitamin B and strychnine. These cholinergic drugs have the property of stimulating the healing of wounds of nerve tissue. Three clinical cases are described in which the results were excellent. The histories of these and 21 other cases which the author treated will be read at the next medical Congress in the United States.

In the after treatment electrotherapy, hydrotherapy, physical therapy, immobilization, and light massage are useful. References are given to American journals in which these experiments are published.

AUDREY G. MORGAN, M.D.

BRAIN AND ITS COVERINGS CRANIAL NERVES

Grimson, K. S., Kernodis, C. E., Jr. and Hill, H. C.: Hypertension. *J. Am. M. Ass.* 1944, 26: 12.

It is well realized that sympathetic surgery for hypertension requires a careful evaluation of each case. The patients who apparently receive the greatest amelioration are those in whom the condition is due to a vasomotor instability, and to which the term "neurogenic hypertension" has been applied. Since the cases due to renal factors have not been relieved, the authors believed it important to evaluate their diagnostic criteria of the effect of rest, sedation, and anesthesia. To this end, a series of tests have been performed on experimental neurogenic hypertension in dogs.

The effect of activity rest, and natural sleep on blood pressure was examined in a group of 4 normal and 4 neurogenic hypertensive dogs. As would be expected a drop in blood pressure occurred during rest and sleep in the normal dogs, and also in 3 of the hypertensive dogs, but in the latter 3 cases it never reached the low levels occurring in the normal dog.

Sodium amytal averaging 0.3 gm. per dog, had no specific effect on the blood pressure of either normal or hypertensive dogs.

Sodium pentothal anesthesia was induced in 5 normal dogs, and in 6 neurogenic-hypertensive and 7 renal hypertensive dogs. This was administered intravenously in a 2.5 per cent solution until pain reflexes were abolished. The results in the normal and renal hypertensive dogs were variable, a rise in blood pressure occurred in about half of the dogs, and a fall occurred in the rest. However 5 of the 6 neurogenic hypertensive dogs revealed a decided drop in blood pressure.

Chloralose anesthesia had no definite effect in either the controls or the neurogenic-hypertensive dogs. Ether anesthesia had little effect on the blood pressure of the normal dogs, but in the neurogenic hypertensive dogs a definite drop in blood pressure occurred in all.

The conclusion is reached that sodium-pentothal or ether anesthesia produced a drop in the blood

pressure of neurogenic hypertensive dogs to approximately the same levels as did rest and natural sleep. Sodium-amytal or chloralose had no specific effect.

The records of 20 patients treated by paravertebral sympathectomy and tested preoperatively for the effect of sodium amytal and rest on their hypertension were reviewed. Although these tests may aid in the evaluation of the hypertensive patient, their importance should not be overemphasized for the results may often be variable and misleading.

JACK I. WOOLY, M.D.

Everts, W. H., and Woodhall, B. The Management of Head and Spinal Cord Injuries in the Army. *J. Am. M. Ass.* 1944, 126, 145.

Head injuries make up 6 per cent of battle casualties. Of these more than three-quarters are closed head injuries with or without simple skull fracture and the remainder are open head injuries.

Closed head injuries receive conservative therapy. During the acute phase in the first seventy-two hours the patient is placed on a modest fluid intake (1,500 to 2,000 cc.) and a light diet. Unless indicated, a lumbar puncture is not done until after from forty-eight to seventy-two hours when it may be desirable to know the pressure and whether or not the fluid is blood-stained. Sedatives are used with caution as they may produce stupor or mask bleeding. Hypertonic solutions are used only when edema is evident and producing symptoms a day or two after the injury. Normal serum albumin is probably the best hypertonic solution. Unless indicated roentgenograms of the skull are not taken until after the first day or two. In some of the forward stations, closed head injuries have been evacuated in ambulatory fashion as soon as the patient was clearly conscious. In general the patient is kept in bed for two or three weeks or more, according to the severity of the injury as estimated from the duration of the period of unconsciousness, the degree of disturbance of the temperature, respiration, and pulse, pupillary abnormalities and focal neurological signs. In a number of the milder head injuries latrine privileges were permitted after the first twenty-four to seventy-two hours and then there was a graduated program of activity over a period of the next ten days with return to light duty in about two weeks and full duty in six. The results in this group were gratifying and the incidence of post-traumatic syndromes was especially low.

All patients with head injuries receive a most painstaking neurological survey in the general hospitals including electro- and pneumoencephalography, mental tests and psychiatric studies. Of a group of 131 patients with closed head injuries 79 per cent returned to full duty after an average hospitalization of twenty-five days, 15 per cent developed post-traumatic syndromes and 6 per cent were still being rehabilitated.

Open head injuries comprise about one-fifth of all head injuries. In two series the mortality was respectively 33.6 per cent and 15 per cent for pen-

etrating wounds and 1 death in 208 and 3 deaths in 224 nonpenetrating wounds. The most important complication is infection, particularly in those cases in which early and complete débridement of the cranial wounds has not been accomplished. In two series fatal infection after operation supervened in 3.7 per cent and 10.8 per cent respectively. Chemotherapy with sulfonamides in fresh wounds does not reduce the incidence of infection when débridement is delayed.

Two new substances, penicillin for the control of infections and fibrin foam for the control of hemorrhage are now receiving clinical trial. In brain abscess surgical drainage must be continued during the period of penicillin therapy as penicillin alone is inadequate. Skull defects in otherwise recovered individuals may be repaired with tantalum plates 0.015 inch in thickness by inlay or other techniques. Before the skull defect is repaired, evaluation of the existing cerebral scar is attempted. Post-traumatic epilepsy has been of minor significance in these cases. Records of cortical electrical activity taken through the tantalum plates are unchanged when compared with preoperative records.

Spinal-cord injuries constitute less than 1 per cent of all battle casualties. Three-fourths were caused by foreign bodies and the other fourth by fracture. Incomplete lesions of the cord were more common than complete lesions (this statement referring to functional and not to anatomic lesions). Sensory examination was the most accurate guide as to the level, and bladder signs were the best guide as to the severity of the lesion; the latter also were good indications for the urgency of operation. Operation was performed in 31 cases, 12 lesions were complete and 19 incomplete. There was improvement in all incomplete lesions operated on and no improvement in any of the complete lesions. Of those in which operation was not performed, 1 incomplete lesion but none of the complete showed improvement. The reasons for operation on complete lesions were cerebrospinal fluid leaks, the presence of block, and x-ray evidence of cord compression. There were 4 deaths all in cases of complete lesions. Death was due to pneumonia and lung abscess in 1 case and to pulmonary emboli in 2 cases; the cause of death in the fourth patient was not ascertained as there was no autopsy. Travel is damaging to cord injuries.

The use of the Stryker turning frame has prevented the occurrence of fresh decubitus ulcers and facilitated the nursing care of the patient. Suspension of the feet, freeing them from contact with the bed clothes and frequent and effortless turning of the patient promote healing of the pressure areas. Change of the bed linen offers no problem on such a frame.

DAVID J. IMPASTATO, M.D.

Grollman, A., and Rousseau, J. P.: Metabolic Craniopathy: Hyperosteosis Frontalis Interna. *J. Am. M. Ass.* 1944, 126, 213.

The authors report a study of 40 patients with the diagnosis of metabolic craniopathy or hyperostosis

frontalis interna. The diagnosis was based upon the history, physical examination, and laboratory studies, and was confirmed by roentgenological findings. These patients were seen at the North Carolina Baptist Hospital, Winston Salem, during the past two and one-half years, and comprised part of a group of 78 patients who on roentgenological examination of the skull, were found to have the calvarial hyperostosis suggestive of this disorder.

The highest incidence as to age distribution occurred in the fourth and fifth decades. The actual age of onset is unknown, however it must have been much earlier in view of the rather benign and insidious character of the condition. There was but 1 male among the patients.

The symptomatology may be grouped into any one or more of the following categories: metabolic, endocrine, hypertensive, or neuropsychiatric. The latter group contained the largest number of patients, but the complaints were extremely variable and did not conform to any definite syndrome. These ranged from minor neurotic complaints to hysteria and major psychosis.

Twenty-three of the patients had metabolic disturbances consisting chiefly of obesity. The basal metabolic rate and blood-cholesterol levels were essentially normal. Hyperglycemia was found in only 3 cases, and in 2 of these it was of a very mild degree. The principal endocrine disturbances were related to abnormalities of menstruation not associated with recognizable pelvic disturbances. Hirsutism was prominent in 12 patients. The 17-ketosteroid excretion was normal in all patients examined in this regard. Hypertension was present in 16 patients, and, although identical with benign hypertensive cardiovascular disease was thought to be another manifestation of the metabolic cranio-pathy.

The typical roentgenological picture of the skull was a hyperostosis of the inner table of the frontal bone. The outer table and thus the external configuration, remained unaltered. Although this was true in all of the cases in this report, other areas of hyperostosis may occasionally be seen in the base of the skull, and in the parietal areas or there may even be diffuse calvarial changes. The frontal bone may attain a thickness of as much as 5 cm. on x ray measurement. Although no specific worth while treatment is known, several of the patients responded favorably to irradiation of the pituitary hypothalamic area. Others so treated had no amelioration of their symptoms.

Despite the absence of a known pathological basis it is the authors opinion that metabolic cranio-pathy is a specific clinical entity of relatively frequent occurrence.

JACK I. WOOLR, M.D.

Dowling, E., Viale, S. M. and Legarreta, C. C.: Peritumoral Meningiomas (Meningiomas peritumorales). *Rev. med. chir. pat. fem.*, B. Afr. 944, 1939.

The author discusses a group of meningiomas originating near the torcular Herophili and compress-

ing the occipital lobe. Two cases are described. The first was in a woman forty-six years of age who for three months had complained of dizziness with a tendency to fall forward. At the same time she began to have difficulty in finding words to express her thoughts. Soon afterward she noticed falling vision and frontal headache followed by nausea and vomiting. Examination of the eyes showed right lower homonymous quadrantanopia with intense edema of the discs and peripapillary hemorrhages. Ventriculography showed displacement of the ventricular system to the right and forward displacement of the posterior part of the left lateral ventricle, the capacity of which was reduced. Operation showed a tumor of the region of the torcular Herophili, which was removed. The patient was well for four months when she returned with a recurrence of symptoms and a second operation showed a tumor in the same region twice as large as the original one. Some months later she returned with another recurrence of the symptoms and inspection showed tumor infiltration of the scalp. She died two months later. The tumor was of the angioblastic type.

The second patient was a man of fifty who had intense pain in the right temporo-occipital and maxillary regions, dizziness, headache, and vomiting. He had once fallen in a canal because he thought there was a bridge across it where none existed. It presented right homonymous hemianopia which did not spare the macular bundle. This, the left hemiparesis, and the electroencephalographic examination indicated that the tumor was not confined to the occipital region but extended into the temporal region as well. A large vascular tumor originating in the peritumoral region was removed. The patient recovered and is well fourteen months later.

The difficulties of diagnosing the occipital localization of these tumors is emphasized. The two leading symptoms of occipital localization are homonymous hemianopia and visual hallucinations. In temporal tumors the visual field defect is supposed to begin in the upper quadrants, while in those of the occipital region it begins in the lower quadrants but often the patients do not come for examination until the homonymous hemianopia is completely established. The visual hallucinations in occipital tumors are supposed to be merely dots and stripes of bright light, while there are more elaborate hallucinations in temporal tumors. However in the author's second case the man believed he saw a bridge over a canal and as a result walked into the canal. The coexistence of cerebellar symptoms indicates a occipital tumor. It is possible that the preservation of the macular bundle and consequently of central vision so frequently seen in occipital lesions masks the falling vision to a certain extent and explains the great edema of the disc and even secondary atrophy which are observed when the patients first come for examination. It is certain that the diagnosis of tumors of the occiput is not on as firm a foundation as that of tumors in other parts of the brain, and generally only a presumptive diagnosis of peritumoral

tumor can be made. About half these tumors are angioblastic and, therefore, particularly malignant.

AUDREY G. MORRAN, M.D.

Hortega, P. del R.: Study of the Oligodendrogliomas (Contribucion al conocimiento de los oligodendrogliomas). *Rev. As. Med. Argent.* 1944, 38, 511.

This is a detailed discussion of the cell structure of the oligodendrogliomas illustrated by photomicrographs of these tumors in the brain, olfactory bulb and optic chiasm. Bailey and Cushing discussed these tumors although they were not sure that they had identified the cells with the oligodendrocytes described by Hortega in 1921.

These tumors occur chiefly in the brain. They are of slow growth, relatively benign and made up of small cells with a round nucleus and a clear cytoplasm. There are four types of normal oligodendrocytes, only two of which, the first and fourth, are found in these tumors. The first is a round cell and the fourth an elongated or Schwannoid type. Contrary to what occurs in the normal cell, the neoplastic oligodendrocyte may adopt different forms and pass from the round to the stellate shape. Among the oligodendrogliomas which the author observed he rarely found cells of a single type; there were not only small round cells but others with numerous processes. Among the tumors that he describes there were at least two types with cells which might be considered oligodendrocytes. In the first most of the cells were undifferentiated morphologically but there were isolated cells or small groups of cells that had the appearance of astrocytes. In the second type most of the cells were differentiated but did not have the appearance of true astrocytes. The latter were cells which developed to a certain extent according to the rules followed by normal cells but never became astroblasts or astrocytes. It is possible that in a single tumor there may be areas that can be classified as astrocytomas while other parts are distinctly oligodendrogliomas.

It is an interesting fact that the only slightly differentiated oligodendrocytes may make the tumor more malignant as they become detached from the tissue and fall into the spinal fluid. They are carried to distant parts and produce metastases. One of the tumors, an oligodendroglioma of the olfactory bulb, followed this course.

AUDREY G. MORRAN, M.D.

SPINAL CORD AND ITS COVERINGS

Shenkin, H. A., and Alpers, B. J.: Clinical and Pathological Features of Gliomas of the Spinal Cord. *Arch. Neurol. Psychiat. Chic.*, 1944, 53, 87.

A correlation of the pathological and clinical features of 27 verified cases of intramedullary gliomas of the spinal cord is presented and an attempt is made to clarify the diagnostic characteristics of these tumors. The cases were evenly distributed as to age from the second to the sixth decade and the tumors occurred predominantly in males. The average dura-

tion of the symptoms in all cases was twenty months. The duration of the symptoms appeared to increase, the lower the position of the tumor in the spinal cord and ependymomas were found to have a distinctly longer course than astrocytomas. It appears therefore that the duration of symptoms cannot be used as a safe criterion in the differential diagnosis of intra and extramedullary tumors.

The first symptom was pain in 16 of the 27 cases, weakness in 7 and paresthesia or numbness in 5 cases. The location of the tumor was apparently of no significance so far as the type of onset was concerned except that with tumors of the cauda equina the onset was always with pain. Severe injury preceded the onset of the symptoms in 6 cases. Because of the conflicting evidence concerning the presence or absence of pain with intramedullary tumor the occurrence of this symptom cannot be used as a differential point in the diagnosis of intra and extramedullary growths. Pain occurred in 23 of the 27 cases and was the outstanding symptom in 18 cases. Root pain was more common than spinal pain while tract pain was least common.

Paresthesias and other sensory symptoms were noted in 23 cases. In all 27 cases there were motor symptoms or signs of varying degree in 9 of which they initiated the picture. Objective sensory changes were present in 14 cases. Sensory dissociation was definite in 8 cases. The objective sensory changes with tumors of the caudal region were insignificant and not in proportion to the subjective sensory complaints. With tumors of the other regions the sensory changes appeared to be significant and of great importance for the accurate horizontal localization of the tumor in the spinal cord. With certain reservations the presence of a waltz-type of sensory disturbance or relatively greater alteration of sensation in the more proximal dermatomes is indicative of an intramedullary process. Less reliable is the dissociation of sensory loss. An indefinite level for sensory loss is of little practical importance in the localization of a spinal tumor within the substance of the cord. The presence of a Brown-Sequard syndrome does not eliminate definitely the possibility of a primary tumor of the spinal cord and contrary to the frequently expressed opinion failure or absence of involvement of the anogenital region does not appear to be characteristic of intramedullary tumors. In 16 cases symptoms of sphincter disturbance were present. Signs referable to the cranial nerves were frequent with tumors which extended as high as the second cervical segment.

In 25 cases manometric studies were made. Complete block was shown in 13 and partial block in 8. In 4 cases with normal cerebrospinal fluid dynamics the thoracolumbar portion of the cord was involved. The most frequent abnormality of the spinal fluid was an increased total protein, the highest values being associated with tumors having the greatest longitudinal extent. Xanthochromia was recorded in 12 instances but the cell count was normal in most cases.

A study of the many contributions concerned with the intramedullary gliomas indicates that the clinical pictures of intra and extramedullary tumors are much the same and that the several points cited for the differentiation of the two conditions are only relatively significant. Despite this the distinction is not clinically difficult when all points are considered. The most distinctive feature of an intramedullary growth is a greater disturbance of sensation in the proximal segments than in the more distal segments.

JOHN L. LUNDQUIST, M.D.

SYMPATHETIC NERVES

Engel, G. L., Romano, J. and McIlwain, T. R.: Vasodepressor and Carotid-Sinus Syncope: Clinical Electroencephalographic and Electrocardiographic Observations. *Arch Int M* 1944, 74, 100.

Syncope or fainting is a transient reaction and it is, therefore, quite difficult to obtain satisfactory reports, especially electrocardiographic and electroencephalographic tracings of patients during an attack. In this article, however, the various types of attacks which can be induced were studied by means of electrocardiograms and electroencephalograms. The work was done in the department of psychiatry in the University of Cincinnati College of Medicine. Eighteen patients and volunteer subjects were studied. Electroencephalograms and electrocardiograms as well as clinical observations were made of the patients simultaneously and suitable complete records are appended to the original article, as well as the clinical data on each case.

Syncope was induced by a variety of means including venipuncture, distention of the duodenum, colon, rectum, or vagina, hyperventilation and the carotid-sinus reflex. The mechanisms of the various types of syncope is discussed. In some instances the distention of the colon was induced by giving large enemas, by inserting a rubber bag and inflating it, or in 1 instance by inserting a duodenal tube and inflating a rubber bag in it. These phenomena are carefully described.

There are two main types of fainting which were discussed: syncope of the vasodepressor type associated with pain, distention of the viscus, venipuncture and other manipulations, and syncope induced by manipulation of the carotid sinus. It was found that vasodepressor syncope could be induced by a variety of stimuli. The surroundings and psychic reaction of the patient are especially important in this variety of syncope. Psychological experiences, such as seeing blood, viewing mutilations, hearing bad news or other emotional reactions strongly predisposed certain people to vasodepressor syncope. Furthermore the vasodepressor reaction may continue for a considerable time after withdrawal of the original stimulus. There results a disturbance in the circulatory apparatus in which there is a discrepancy between the volume of the vascular bed and the volume of the circulating blood. In most instances

this can be overcome by gravity, hence, the advantage of collapse and falling to the ground. Certainly the erect posture of the patient was unsatisfactory.

The symptoms and signs of vasodepressor syncope, such as pallor, sweating, weakness, nausea, and faintness are secondary to the fall in arterial blood pressure. This was shown by the prompt improvement in a recumbent position, when the blood pressure rose. Even though the persistence of the functional disturbance could be repeatedly demonstrated by returning the subject to the erect position, in some cases the disturbance continued even with the patient in the recumbent position and the authors find it difficult to say at what stage this condition of persistent hypotension passes into a condition which could be described as primary shock. Unconsciousness in vasodepressor syncope is a late phenomenon and occurs only when the arterial blood pressure has been extremely low.

Recovery from vasodepressor syncope may take place in the erect position, but the subject should be encouraged to lie down and, especially, to move the legs with a certain amount of activity and then should be gradually restored to the erect position. However, he should be warned against remaining motionless standing, or even sitting. The old remedy of slapping the face and throwing cold water on the individual has a sound theoretical foundation as it provokes resistance and muscular activity.

With regard to the electroencephalographic findings in these cases, slow waves invariably appeared in the electroencephalogram in any case of syncope which was allowed to progress to unconsciousness. Furthermore recovery from complete unconsciousness always took place in a certain definite way: (1) the waves decreased in amplitude, (2) there was random low voltage and fast activity and (3) low amplitude regular waves occurred which rapidly reached alpha frequency. These stages, occurring over a course of seconds or minutes are essentially the same as those observed during recovery from delirium over the course of days or weeks. In 3 cases of the cerebral type of carotid-sinus syncope the development of contralateral focal neurological signs and symptoms without loss of consciousness was associated with abnormal waves from the ipsilateral cortex.

Another report which is being prepared by the authors will show that hysterical syncope is not accompanied by any slow waves in the electroencephalogram. Hyperventilation was also used to produce syncope, again with the appearance of slow waves in the electroencephalogram.

ADRIEN VERBROEGHE, M.D.

Smithwick, R. H.: The Surgical Treatment of Hypertension: The Effect of Radical (Lumbodorsal) Splanchnicectomy on the Hypertensive State of 154 Patients Followed Up For from One to Five Years. *Arch Surg* 1944, 49, 40.

The author has thoroughly reviewed his series of 156 hypertensive patients operated upon during the

past five years. The lumbodorsal splanchnicectomy as originally advocated and now known as the Smithwick sympathectomy was used. The extent of the denervation varied but in all of the cases the great splanchnic nerves were removed from the celiac ganglion to at least the midthoracic level. No correlation has been drawn in this report between the extent of the operative procedure and the results. The operative mortality rate was 2.8 per cent.

A gross tabulation of the results of splanchnicectomy has been made from changes of the diastolic blood pressure. This is shown in Table I.

The period of reduction in blood pressure following operation is still unknown. However, a comparison between two-thirds of the patients followed up for approximately two years and one third of the patients followed up for approximately three years has not revealed a significant difference.

By further dividing the patients on the basis of the pulse pressure three types of hypertension have been derived. Type I is that group having a pulse pressure of less than one half the diastolic blood pressure. Type II having a pulse pressure up to 10 mm. more than one half the diastolic pressure and Type III having a pulse pressure 20 mm. or more greater than one half the diastolic pressure. This grouping has given a very interesting and helpful prognostic criteria in that the patients with the smallest pulse pressure, on a percentage basis, had the best results while those with the highest pulse pressure had less favorable results.

The sex factor is of interest since 84.8 per cent of the women and only 71.8 per cent of the men were definitely benefited.

A point worthy of further study is the correlation of renal pathology with results of the operation. Renal biopsy material of 100 patients was classified and grouped into that of patients with none to mild changes and that of patients with advanced degrees of arteriolar disease. However, there was essentially no difference in response to surgery. An unusual finding was that of 11 patients with pyelonephritis, 90.1 per cent had excellent results while 100 per cent had some benefit. Glomerular filtration was reduced about 20 per cent immediately after operation, however it returned to normal within one year. Studies of kidney function revealed that the majority of patients had some improvement after operation as adjudged by clearance of sediment, disappearance of albumin and improvement in concentration.

Hypertensive funduscopic changes were correlated with the splanchnicectomy and it was found that in the more advanced cases improvement of the fundus picture was more likely to occur. Among the most severely damaged cases, improvement occurred in 100 per cent. It should be noted that of the group of patients who did not obtain a satisfactory drop in blood pressure, 48.2 per cent revealed an improvement in their eyegrounds.

An electrocardiographic study before and after operation revealed an improvement in 63.5 per cent of the records of two-thirds of the patients who had

TABLE I.—EFFECTS OF LUMBODORSAL SPANCHNICECTOMY ON THE BLOOD PRESSURE OF ONE HUNDRED AND FIFTY SIX PATIENTS FOLLOWED FROM ONE TO FIVE YEARS*

Result group	No. of patients	Percentage	Effects of lumbodorsal splanchnicectomy	
			Effect on diastolic blood pressure	Average reduction
	64	65 70.4	Lowered 20 mm. or more	6/43
	32		Lowered 10 to 20 mm.	44/34
	8		Lowered 1-9 mm.	7/3
	7	9 20.6	Lowered 1-9 mm.	0/5
	5		Increased	(Increase) 8/
Total	56			

Average three followed, twenty-two and half months. In this table the results are considered as a whole. They have been subdivided into six smaller groups according to type of blood pressure and sex (Tables 2, 3 and 4). When subdivided in this fashion, the results are much more helpful in indicating the outlook for the individual patient than when they are undivided, as in this table.

definitely abnormal records. Again it is worthy of note that of the patients not obtaining satisfactory blood-pressure responses, 55.9 per cent showed an electrocardiographic improvement.

It therefore appears that the present available methods of study do not give full value to the beneficial results derived from splanchnicectomy as measured by a change in blood pressure.

JACK I. WOOLR, M.D.

Rojas F. Smithwick, R. H. and White, P. D.: Nonspecific Major Operations and Lumbodorsal Sympathectomy. *J Am Med Ass* 1944, 126: 15.

In 1939 Volini and Flaxman followed the course of the blood pressure of 17 hypertensive patients operated on for different reasons not related to their hypertension. They observed in almost every case a postoperative reduction in the blood pressure and concluded that the blood pressure reduction attributed to nerve resection was actually due to the conditions brought about by the major operations. On this basis they denied the specific effect of sympathetic-nerve resection on hypertension. In 1943 Adamson and Dubo arrived at similar conclusions.

With the purpose of checking these opinions the authors studied the records of 100 hypertensive patients who had been submitted to various major operations (Group 1) and of another 100 hypertensive patients who had submitted to bilateral lumbodorsal sympathectomy by the procedure of Smithwick (Group 2).

This study shows that nonspecific major operations produce some immediate reduction of the blood pressure of hypertensive individuals (Table I). How

TABLE I—IMMEDIATE EFFECT OF OPERATION

	No results	Moderate reduction	Pronounced reduction
Group 1. Immediate reduction (up to 6 months after the operation)			
Systolic pressure	49%	40%	2%
Diastolic pressure	60.3%	27%	2.6%
Group 2. Immediate reduction (4 days after the second stage of the operation)			
Systolic pressure	3.3%	24.4%	72.3%
Diastolic pressure	8.8%	37.7%	53.5%

TABLE II—CONDITION SIX OR MORE MONTHS LATER

	No results	Moderate reduction	Pronounced reduction
Group 1. Late reduction (more than 6 months after the operation average period of observation, months)			
Systolic pressure	82.7%	17.3%	0%
Diastolic pressure	36%	14%	0%
Group 2. Late reduction (more than 2 months after the second stage of the operation average period of observation, 30 months)			
Systolic pressure	9.6%	28.1%	62.3%
Diastolic pressure	7.6%	36.1%	56.3%

ever this reduction is not pronounced and in most cases persists for only a short time (Table II). In the majority of cases lumbodorsal sympathectomy produces pronounced reduction of the blood pressure, which is still present after a considerable period of time (Tables I and II). DAVID J. INFANTATO, M.D.

MISCELLANEOUS

Gurdjian E. S., Webster, J. E. and Stone, W. E.: The Cerebral Metabolism in Experimental Head Injury. *Wor Med Chic* 944 6 73

An experimental study was conducted to ascertain the effects of head injury on the cerebral oxidative metabolism. Experimental injuries were made on dogs, following which blood specimens were obtained from the femoral artery and the femoral and external jugular veins and were compared with specimens taken previous to the blow. The longitudinal sinus was also exposed, and specimens were taken from this region, following which the brain was further exposed and frozen *in situ* with liquid air. Oxygen levels and carbon-dioxide and oxygen capacity of the blood were determined, as well as the blood level of dextrose and the lactic-acid level in the brain.

The most common observation in this series of experiments was that of increased oxygenization after injury to the head. No significant changes were

noted in the cerebral arteriovenous difference in oxygen. The carbon-dioxide values were about the same as in the control animals. The areas of the cortex showed no macroscopic evidence of contusion, and often appeared entirely normal as regards the chemical constituent studies, even in profoundly injured animals. Areas of cortex which had sustained visible contusion showed marked chemical changes roughly proportional to the degree of local damage, but they did not bear relation to the physiological response. The chemical changes consisted of increase in lactic acid, loss of phosphocreatine and adenosine triphosphate and some increase in inorganic phosphorus.

A study of the effect of oxygen inhalation on brain contusion was conducted. The result would indicate that the administration of oxygen induces no pronounced acceleration of recovery processes, but does seem to produce a trend toward better recovery.

Observations in this study would indicate that the chemical changes in the areas of brain contusion are comparable to the changes observed in cerebral anoxia and in cerebral tissue after death.

Delayed experiments and studies were made after the lapse of several days following injury and improvements were found to have occurred in the oxidative processes in areas of contusion, as evidenced by return toward normal levels of the chemical constituents that were studied.

HOWARD A. BROWN, M.D.

Gurdjian E. S. and Webster J. E.: Acute Physiological Responses in Experimental Head Injury with Special Reference to the Mechanism of Death Soon after Trauma. *Surgery* 944 16 34

In this report the changes in blood pressure, the pulse and respiration, the conscious state, and the reflexes immediately following trauma to the head are considered in detail. The mechanism of death soon after trauma is also analyzed. Dogs morphinized for analgesia were used in the experiments. A variety of preparations were made prior to head injury in different animals: spinal-cord section at the first thoracic level; bilateral adrenalectomy; bilateral vagus-nerve section and carotid-artery ligation and section. Intravenous administration of yohimbine to remove the influence of the sympathetic system, and bilateral supratentorial exposure of the brain. Electroencephalographic studies were made in 9 animals and the findings were analyzed with reference to medullary function.

The acute responses to injury are divisible into 3 types: (1) minimal, (2) moderate, and (3) profound. In moderate and profound injuries there is usually a sudden increase in blood pressure with respiratory loss, unconsciousness, loss of corneal reflexes, and frequent generalized rigidity followed by flaccidity. In moderate injuries the animals survived or died, while in the group with profound injuries they almost always died. Under morphine analgesia the ability to respond to pain was considered an adequate sign of consciousness. Loss of the corneal reflexes repre-

sents a more profound response to injury than unconsciousness.

Evidence of vagal paralysis was common in moderately and severely injured animals but in some there was evidence of vagal stimulation and bradycardia. In the group of animals in which the vagi and carotid arteries were sectioned injury to the head caused responses similar to those seen in the intact animal except that there was no change in the pulse rate. In adrenalectomized animals injury caused the usual rise in blood pressure associated with respiratory failure. It was believed that the increase in blood pressure in this group was not mediated by a humoral factor (adrenalin liberation). In animals with previous spinal-cord section and resulting low blood pressure severe head injury with eventual profound effect was never associated with hypertension. It seems reasonable to assume that if the spinal cord had been intact there would have been the usual acute hypertension following trauma. When an animal was given an amount of 3 ohimbine sufficient to prevent a rise in blood pressure on injection of $\frac{3}{4}$ cc. of adrenalin solution injury to the head was never associated with an increase in blood pressure. These two groups of experiments suggest that the sympathetic nervous system mediates the acute peripheral hypertension which is encountered in head injury.

In several animals with bilateral craniotomy and exposure of the brain a supratentorial bullet wound never caused a pressor effect, although the injury was severe. This indicates that the increase in blood pressure is brought about by medullary stimulation and not by stimulation of the supratentorial cortical

or subcortical centers. In 4 animals the medulla or spinal cord was injured by gunshot. In 2 animals in which the region of the obex was destroyed the pressor effect did not appear. In 2 animals with injury lower down, a marked pressor response appeared in one and an increase in pulse pressure in the other. It is apparent that a dissolution of the vasomotor center itself causes the death of the animal while if the vasomotor center is allowed to remain intact with energies acting upon it from a distance, its first discharge is one of peripheral vasoconstriction with consequent increase in the blood pressure. It is conceivable that in some experiments a depressor mechanism may be the cause of a drop in pressure but paralysis of the vasomotor center itself is usually the cause of circulatory failure and death. The presence of intracranial vasodilatation with peripheral vasoconstriction need not necessarily be construed as evidence of traumatic stimulation of a depressor mechanism since it may happen with any other factor causing peripheral vasoconstriction.

Respirations were affected in a multitude of ways. In general the respiratory response did not appear to be dependent upon vasomotor activity. Respiratory paralysis is a direct result of injury to the respiratory center. The respiratory center or the vasomotor center or both may be affected by trauma.

Electroencephalographic changes did not correlate with medullary involvement. Evidences of medullary paralysis could be obtained without a simultaneous inactivity of the brain waves and conversely in some animals the electrical activity of the brain failed in the presence of respiration and corneal reflexes.

JOHN L. LINQUIST, M.D.

SURGERY OF THE THORAX

TRACHEA, LUNGS, AND PLEURA

Pierson, P. H.: Primary Carcinoma of the Trachea. *J Am Med Ass* 1944, 126: 206

A man of sixty-one who had intermittent bouts of severe cough dyspnea suffocation and moderate hemoptysis for three years was found to have a primary adenocarcinoma of the trachea. An attempt to prove the histogenic origin from an aberrant thyroid by the use of radioactive iodine was unsuccessful. After removal of as much as possible of the tumor through the bronchoscope the remnant was treated with radium applied within the trachea. Two years after treatment there are no subjective or objective evidences of tumor. HOWARD A. MCKENNEY, M.D.

Jones, J. C., and Thompson, W. P.: Arteriovenous Fistula of the Lung. *J Thorac Surg* 1944, 3: 357

In a single white woman, twenty-four years of age, a provisional diagnosis of arteriovenous aneurysm of the right lung was made on the history of cyanosis since birth, the persistent secondary (or symptomatic) polycythemia, the presence of a continuous murmur over the tumor mass in the right lung, clubbing of the fingers, and a normal heart. Later planigraphic studies indicated that there were several masses in the right lung instead of the one tumor mass indicated by the ordinary roentgenogram, that their arterial vascular supply might be separate from those of the upper and lower lobes and that the tumor masses might be made up largely of dilated branches of the pulmonary artery going to the right middle lobe.

After a few months of tentative collapsing of the right lung by means of pneumothorax, the chest was opened through a curved inframammary incision, extending from the third intercostal space anteriorly under the right breast and upward and laterally to the third rib in the midaxilla. There was no semblance of a middle lobe roughly corresponding to where the middle lobe should normally be; there was attached to the anterior and inferior aspects of the upper lobe a reddish-blue pulsating mass the size of a lemon with a paper thin wall. Tapes were passed around what appeared to be the pulmonary artery which was large and dilated, and around the inferior pulmonary vein. No superior pulmonary vein was seen, either at operation or in the specimen after ward. Occlusion of the pulmonary artery suppressed the pulsation in the mass, and occlusion of the inferior pulmonary vein caused the tumor to become larger and more distended. It also caused some superficial varicosities over the surface of the upper lobe to become more prominent. This direct communication between the pulmonary artery and the inferior pulmonary vein was shown, after removal of the lung, on the operatively removed specimen by the

injection of a bismuth medium through the inferior pulmonary vein directly into the pulmonary artery supplying the tumor mass and from here on into the arterial branches supplying the entire lung.

A right total pneumonectomy was done by dissection and individual ligation: first, the pulmonary artery was cut between transfixion sutures, then the inferior pulmonary vein; finally the lung was suspended distal to a clamp applied to the right main bronchus. The right bronchus was closed with right over-end single stainless steel, 35-gauge wire suture, which were tied after the clamp was removed. The mediastinal pleura was closed after thorough irrigation of the stump and of the pleural cavity with saline solution and after 5 gm. of sulfanilamide crystals were sprinkled over the bronchial stump. The ribs were brought together with pericostal sutures and the chest wall was closed in layers without drainage.

Following the operation the cyanosis disappeared within a few hours, the wound healed per primam, and the blood picture returned to normal within a few days. Four months later the patient was well, active, free of dyspnea and cyanosis; the physical findings were completely normal with the exception of clubbed finger ends, and this finding was definitely less in degree. Fluoroscopy showed the right chest to be almost filled with fluid above which was air.

In the discussion ADAMS presented lantern slides showing the photographic appearance, roentgen studies and blood and oxygen studies of a male workman, twenty-four years of age, suffering from repeated attacks of epistaxis, with marked cyanosis, and clubbing of the fingers and toes. Following operation there was an immediate fall in the red-cell count and hemoglobin content and a restoration of oxygen values to approximately normal.

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BROOK tentatively suggests the possibility of closing the fistula by ligation of the pulmonary artery. In this connection, however, JONES, in his closing statement, said that he would rather sacrifice the lung in this case than attempt to dissect out any of the branches or even to leave the lung in and ligate the pulmonary artery. JOHN W. BURNHAM, M.D.

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SURGERY OF THE THORAX

TRACHEA, LUNGS, AND PLEURA

Pearson, P. H.: Primary Carcinoma of the Trachea. *J. Am. Med. Ass.* 1944, 26: 806.

A man of sixty-one who had intermittent bouts of severe cough, dyspnea, suffocation and moderate hemoptyses for three years was found to have a primary adenocarcinoma of the trachea. An attempt to prove the histogenic origin from an aberrant thyroid by the use of radioactive iodine was unsuccessful. After removal of as much as possible of the tumor through the bronchoscope the remnant was treated with radium applied within the trachea. Two years after treatment there are no subjective or objective evidences of tumor. HOWARD A. MCKINTOCK, M.D.

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The characteristics of the chyle were studied by the author. The infant survived slightly over two months, during which time a total of 5,300 cc. of chyle were removed. The total protein varied from 2.72 to 2.97 gm. per cent the albumin globulin ratio was about 4 to 1. This severe protein loss required intensive therapy consisting of blood plasma and chyle transfusions.

In adults some observations have been recorded on the intravenous administration of chyle. Four of 9 cases were improved in 3 no response was obtained and in 2 cases sudden death occurred, possibly due to an anaphylactic reaction. This patient received a total of 14 chyle infusions ranging from 60 to 100 cc. in volume without reactions. The authors believe that reactions could hardly be due solely to anaphylaxis as chyle normally enters the blood stream. The extensive loss of protein fat, and electrolytes through repeated aspiration of chyle warrants the intravenous use of the fluid removed. No cause for the effusion was found in this patient.

THOMAS F THORNTON JR. M.D.

Sampson H. H. and Collis J. L.: Postlobectomy Lobar Collapse. *J Thorac Surg* 1944 13 435

Since lobectomies have been performed for bronchiectasia postoperative collapse of the remaining lobe on the same side has been a perpetual stumbling block in the path of good results. Postoperative collapse may cause increase in mortality prolonged convalescence, or a poor result. Poor results are due to the development of bronchiectasis in the collapsed lobe. One such case is cited by the author.

Secondary collapse has been attributed to such factors as reflex bronchial spasm, swelling of the mucosa due to bronchography, swelling of the stump or the absence of adhesions to aid in expansion of the lobe. Certain bronchoscopic observations made by the authors have led them to advance another theory. At bronchoscopy swelling of the hilum was not noted. The collapse always appeared to be caused by obstruction with sputum and re-expansion of the lobe always occurred when the sputum was removed. Finally when the lower lobe is removed, the upper-lobe bronchus is found to open almost directly upward so that it is parallel to the stump of the lower lobe bronchus. This is due to expansion of the upper lobe in an effort to fill the cavity produced by removal of the upper lobe. In a patient who has an ineffective cough due to pain the

stump easily fills with pus which spills over into the upper lobe. The extent of symptoms depends entirely upon how much pus works into the smaller bronchi.

In practice, bronchoscopy has provided satisfactory treatment. In adults usually one bronchoscopic examination suffices although it may have to be repeated in children. The authors have observed 12 cases of postoperative collapse in 33 cases of lobectomy. All have responded well to bronchoscopy. To date postural drainage has been the only method of prophylaxis that has reduced the incidence of the condition.

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The authors have adopted Head's technique for use in far advanced cases and in those with mixed emphysema. Cosmetic and functional results are improved because of small incisions and because the muscles of the shoulder girdle are not severed. In mixed emphysema the infected field may be avoided until the final stage is performed.

Since 1942 the authors have performed 79 stages upon 31 patients with mixed emphysema or for advanced cavernous disease. Results were uniformly good except in 2 patients with extensive bilateral disease. Modifications of the instruments and technique are discussed.

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There is some difference of opinion as to which side should be operated on first but most surgeons prefer to operate on the side that is in the worst

condition. The first operation is borne better by the patient and the treatment of the worst side may have a favorable effect on the disease in the other side—it may even render operation on that side unnecessary. At any rate when the lesions on the first side are cured operation on the other side is less dangerous.

German, Argentine and Brazilian surgeons prefer to operate under local anesthesia by infiltration with 0.5 per cent novocain with adrenalin added. The American, French, English and Scandinavian surgeons use general anesthesia with gases. The authors believe that local anesthesia permits closer observation of the respiratory condition during the operation.

It is best to divide the bilateral operation into several stages: the arches of not more than three or four ribs being resected at one time. In the second operation the greatest care should be taken not to reduce the respiratory field too suddenly. Total resection of the first three ribs followed by extrafascial apicolysis by Semb's method should be the first stage in the second thoracoplasty. This extrafascial apicolysis is an indispensable means of furthering collapse of the apex and often reduces the number of ribs that have to be resected. The interval between the two operations must be long enough to permit reossification of the periosteum.

The authors describe 4 cases they have operated upon and illustrate them with roentgenograms. In the first the indication was primary that is both upper lobes were involved at the time of the first operation. In the others it was secondary that is the lesions in the second lung developed after the first operation. In the first operation they resected the whole of the first and second ribs and then after a few minutes observation of the respiration, pulse, and blood pressure, they resected the arcs of the other ribs down to the fifth. Too much of the fifth rib should not be resected. In 2 cases they used Semb's technique with resection to the fourth rib. In both of these cases they had excellent collapse without serious disturbance of the circulation. In 1 case in which the patient's general condition was serious, a resection to the sixth rib had been performed previously. They resected to the fifth rib on the other side in two stages and the results were good. In the only case in which they operated under general anesthesia they were able to resect only to the third rib on account of intense tachypnea. The amount of collapse obtained in this case was insufficient.

In their first case the interval between the operations on the first and second sides was only two weeks, the shortest interval known. In this case there was an intense fibrous reaction and pronounced rigidity of the mediastinum, and the extent of the lesions and the amount of expectoration necessitated the second operation in the shortest possible time. The course in this case was the most favorable of any case they have seen.

AUDREY G. MORGAN, M.D.

HEART AND PERICARDIUM

Taylor, H. A. and McGovern, T.: Angiocardiography: Anatomy of the Heart in Health and Disease. *Radiology* 1944 43 364.

Angiocardiography had its beginning in 1921 when Robb and Weiss started their studies on cardiac physiology and circulation time. At present the method in use is the result of investigations by Forsman, Castellanos and Robb. This type of examination affords a means of determining the size and shape of the heart, the presence or absence of cardiac hypertrophy, chamber enlargement, or both, also the location of the valves and the position of the chambers, the ventricular conus, the pulmonary aorta and its branches, the aorta, and the border forming structures of the cardiac silhouette.

The normal appearance of the heart chambers and the large vessels is described as are the changes observed in size and shape in cardiac patients. The study is based upon observations made on 370 persons, 13 of whom were normal, the remainder had some form of cardiovascular disease. Certain variations from the accepted roentgenographic picture of the normal cardiac silhouette were demonstrated. The middle cardiac segment is formed most often by the left pulmonary artery. Infrequently by the pulmonary aorta, and sometimes by both. The descending aorta may also participate. The conical conus is deeply situated. It is never a border forming structure and is quite removed from the middle cardiac segment.

THOMAS F. THORNTON, JR., M.D.

Proescher, F. and Haumann, F. W.: Abnormal Origin of the Left Coronary Artery with Extensive Cardiac Changes in a Female Child Thirteen Months Old. *J. Pediat.*, St. Louis, 944 35 344.

A case of abnormal origin of the left coronary artery is reported. The patient was a thirteen-month-old female child who had a history of repeated attacks of fever, coughing and wheezing. The patient was admitted to the hospital because of one of these attacks. Physical examination showed flatness of the left lower chest, decreased breath sounds, and crepitant rales. The clinical diagnosis was pneumonia of the left lower lobe of the lung. The child died suddenly fifteen hours after admission.

Autopsy revealed a greatly enlarged heart which occupied the left lower thorax and caused the lower lobe of the lung to be completely atelectatic. The heart was 11.5 by 7.5 cm. and weighed 180 gm. The normal weight of the heart for an infant of this age is about 42 gm. The increased size of the heart was due to left ventricular enlargement. The right coronary artery originated from the right sinus of Valsalva. It was normal in size and had a normal distribution. No vessel originated from the left sinus of Valsalva. Instead the left coronary artery originated from the left pulmonary artery about 1 cm. above the valve. Its orifice was pinpoint in size and

it represented the entire blood supply to the left ventricle as there was no anastomosis between the right and left coronary arteries.

The histological findings were different from the so-called genuine hypertrophy in which there is an increase in the muscle fibers without degenerative changes. In this case there were extensive degenerative changes with replacement by connective tissue and calcification.

The case herein reported brings to 18 the number of infants in whom this anomaly has been reported.

FORESTER D. DOORILL, M.D.

Harrington, S. W.: Chronic Constrictive Pericarditis: Partial Pericardiectomy and Epicardiectomy in 24 Cases. *Ann. Surg.* 1944, 120: 468.

Chronic constrictive pericarditis is the term most generally accepted to designate an inflammatory lesion of the pericardium and epicardium in which fibrous adhesions often associated with deposits of calcium and occasionally pockets of encapsulated fluid form on and between these coverings of the heart, and in which the inflammatory scar contracts around and onto the heart muscle to such a degree that it interferes with the normal diastolic and systolic functions of the heart and causes impairment of the circulation.

The two most common conditions with which constrictive pericarditis is most likely to be confused clinically are cirrhosis of the liver and congestive heart failure from intrinsic cardiac disease. In most instances, however, the subjective symptoms of constrictive pericarditis are sufficiently characteristic so that when they are correlated with the physical and laboratory findings a definite diagnosis can be established.

The development of factors which produce the clinical syndrome of constrictive pericarditis is slow but progressive. The amount of blood entering the heart and being pumped into the circulation by the heart per beat and per minute gradually decreases. This decrease results in low blood and pulse pressure, faint heart sounds, tachycardia, a paradoxical pulse, and auricular fibrillation. The back pressure on the venous circulation results in high venous pressure, dilatation of the veins, enlargement of the liver and transudation of fluid into the tissues of the body, particularly into the abdomen and pleural cavities, as well as into the tissues of the extremities and face.

The number and severity of subjective symptoms increase progressively with the course of the disease, the earliest symptoms are general weakness and fatigue. Dyspnea is noted on exertion and usually is relieved by rest, particularly by lying down. Orthopnea is experienced rarely. Digestive disturbances such as anorexia, epigastric distress, and fullness in the abdomen after meals, usually are not noticed until after the liver is enlarged considerably and probably they can be attributed to hepatic damage for these symptoms seem to be more severe in cases in which the tests of hepatic function reveal a con-

siderable degree of retention of dye. Swelling of the abdomen does not occur early in the course of the disease, however, it may be one of the first symptoms noticed by the patient. When ascites develops it usually becomes progressively more extensive. Edema of the extremities which may extend to the face and neck usually does not occur until after ascites has been present for some time. When venous congestion has advanced to this degree the entire venous system usually is dilated markedly. This dilatation is particularly noticeable in the veins of the cervical region. The effects of this condition cause increasing disability which gradually becomes total disability unless surgical relief is obtained.

The laboratory findings in chronic constrictive pericarditis give valuable aid in establishing a definite diagnosis. The venous pressure is elevated above normal. The circulation time of the blood is increased. The tests of hepatic function indicate a varying degree of hepatic damage which depends to some extent on the duration of the disease.

Röntgenological studies of the heart in cases of constrictive pericarditis usually reveal it to be normal or smaller than normal, occasionally slightly enlarged but never markedly enlarged or segmentally dilated as in congestive heart failure from intrinsic cardiac disease and hypertensive heart disease. The presence of calcareous plaques in the pericardium is noted frequently. This is always suggestive of the possibility of a constricting pericardium but calcium may occur in the pericardium without other findings of constrictive pericarditis.

The preoperative preparation of patients who have been selected for surgical treatment is directed at removing the effects of the circulatory failure from the constriction of the heart and at improving the function of the structures involved.

The intake of fluid should be limited to from 1,200 to 1,500 cc. in twenty-four hours. Patients should receive a diet high in protein and low in salt. Daily administration of vitamins may be of value in improving the general resistance of the patient. When tests of liver function indicate considerable damage vitamin B complex and glucose administered intravenously or by mouth may be helpful in improving the function of the liver.

The body cavities and tissues should be relieved of as much excess fluid as possible. When large amounts of fluid are present in the abdominal and pleural cavities the fluid should be removed by aspiration and periodic use of diuretics should be made to relieve edema of the tissue and keep it at a minimum.

The value of preoperative administration of digoxin is questionable.

The level of blood urea, plasma chlorides and serum protein and the carbon-dioxide-combining power of plasma are determined routinely before operation to see that they are within normal limits as well as for control of the postoperative determinations. The type of the patient's blood is determined and blood of similar type is held available for intrav-

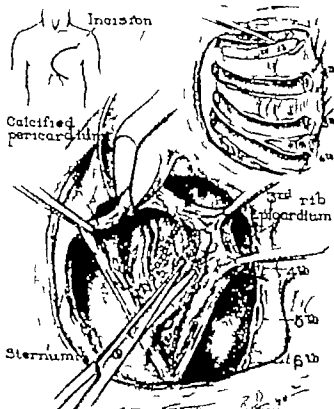


Fig. 1 Sharp dissection of the constricting epicardium (pericardiolysis) and pericardium from the myocardium. Bone cutters were required for resection of the scar because of the thickness of the calcification. Left inset, U shaped precordial incision. Right inset, Approach to the pericardium through the wall of the thorax. Resection of the cartilages and 3 cm. of the third, fourth, fifth, and sixth ribs on the left side (resection proximal half of sternum)

but to shift into another line of cleavage and then separate the intervening bands to avoid myocardial injury

An attempt is always made to free the left ventricle first because better function of this chamber of the heart should be established to provide better disposal of the blood before freeing the right side of the heart. In many instances however the author has separated the greater portion of the right ventricle first without harmful effects.

Opinions differ concerning the amount of pericardial scar that it is necessary to remove as well as the amount of scar to be separated from the heart muscle and from the orifice of the inferior vena cava. The author believes it is advisable to separate as much of the pericardial scar as possible from the ventricles the right auricle and orifice of the inferior vena cava and it is of particular importance to separate the attachment of the right ventricle to the diaphragm. It is of equal importance to separate the apex of the heart, and the author believes that this should be done early in the operation if possible. Separation of the heart muscle from its fixed attachments to the diaphragm is one of the most important considerations in reestablishing the action of the heart. Improvement in the function of the heart

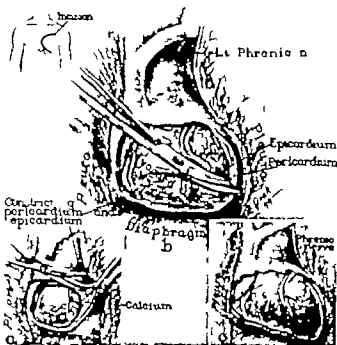


Fig. 2 Resection of, and marginal incisions in, the pericardium and epicardium after separation from the myocardium. Inset a, Beginning resection of the pericardial scar from the anterior and larger surface of the myocardium. b and inset c, After resection of the pericardial scar multiple incisions are made into the cut margin of the remaining epicardium and pericardium to release the heart more fully particularly at the apex. (Courtesy of J. B. Lippincott Co.)

often is noted immediately after the apex and right ventricle have been separated from their fixed attachment to the diaphragm.

After the scar has been separated from the heart muscle the amount of pericardium to be resected depends on the character of the scar and the position and type of fixation of the pleural attachments to the outer wall of the pericardium. The author believes it is advisable to resect as much of the anterior portion of the pericardium as possible without injury to the pleura. By careful dissection the pleural attachments to the pericardium can be separated to approximately the position of the left phrenic nerve and the entire anterior portion of the thickened pericardium extending beneath the sternum is resected. If the attachments of the pleura extend high on the pericardium, as they often do when calcium is present, it may be impossible to resect an adequate amount of pericardium without injury to the pleura. In these cases linear incisions into the remaining cut edges of the pericardium will produce a much wider opening of the pericardium.

The importance of separating and removing sufficient scar to release the heart cannot be overestimated because if an adequate amount is not removed cardiac action will continue to be impaired. This not only will eliminate the possibility of ultimate recovery from the disease but will interfere with the immediate recovery from the operation.

In the course of removal of the pericardial tissue the pulse rate often becomes rapid and irregular because of the external stimulus to the heart muscle. When the pulse becomes irregular it is important to cease the operation temporarily. The utilization of frequent rest periods and applications of sponges moistened with warm physiological solution of sodium chloride will permit the heart to regain or at least partially regain its former rhythm.

The upper half of the wound down to the bed of the cartilage of the fifth rib is closed in two layers. Above the cartilage of the fifth rib the intercostal muscles are sutured to the sternum. The perichondrium of the cartilages of the fifth and sixth ribs is excised completely. From the cartilage of the fifth rib to the lower angle of the wound the subcutaneous tissue and skin only are closed over the heart. Soft rubber tissue drains are placed in the lowermost angle of the wound between the heart and the diaphragm. These drains permit the immediate removal of the serous exudate from the precordial space. The drains are removed from thirty-six to forty-eight hours after operation.

A varying amount of serous exudate always follows removal of the adhesions, even though great care is taken to prevent trauma to the tissues as well as to attain accurate hemostasis. If this fluid is permitted to accumulate in the precordial space it may interfere with the function of the heart which is already laboring under increased stress from the operation. If it is not permitted to drain externally, the fluid may rupture into the pleural space and interfere with respiratory function. When granular deposits of calcium are scattered throughout the pericardium, it is particularly advisable not to have this material drain into the pleural cavity because of the risk of pleural irritation and empyema.

Immediately after operation all patients are placed in oxygen tents. The time during which the administration of oxygen is continued depends on their progress. This is one of the most important aspects of postoperative treatment for the oxygen not only prevents cyanosis but aids in relieving stress on the heart. Other postoperative measures are directed toward removal of body fluids and aiding the function of the heart and liver. These measures are similar to those utilized preoperatively for similar purposes. Limitation of the intake of fluid is important from 1,200 to 1,500 cc. of fluid is administered in twenty-four hours by proctodysis or by mouth as soon as nausea subsides. The intravenous administration of fluids is avoided if possible. In instances in which the urinary output is reduced from 10 to 20 per cent solution of glucose may be administered intravenously. This not only aids the urinary output but may benefit the function of the liver. Vitamin B also is given.

In 24 cases the operative mortality was 25 per cent. Of the 15 patients who recovered from operation 9 are considered "cured" in the sense that subjective symptoms were relieved and the patient was rehabilitated to his former or some other useful

occupation. The improvement of 2 in 24 patients has approximated a cure. In 2 other cases a 3rd operation was recent, improvement has been progressive. Thus 13 of this series of 24 patients ultimately may be considered as cured. Of the remaining 5 patients who recovered from the operation 2 have shown moderate improvement and 3 died. Two of these deaths were due to continuation of the disease and 1 was due to pneumonia.

ESOPHAGUS AND MEDIASTINUM

Haight, C.: Congenital Atresia of the Esophagus with Tracheoesophageal Fistula: Reconstruction of Esophageal Continuity by Primary Anastomosis. *J. N. Surg.* 944, 120-614.

Congenital atresia of the esophagus is found at a level corresponding to the junction of the upper and middle thirds of the esophagus. The upper part of the esophagus ends as a blind pouch in almost all instances. The upper end of the lower esophageal segment usually enters the trachea, thus forming a tracheoesophageal fistula; this occurred in 22 of the 31 patients in the author's series. The condition is incompatible with life as feedings cannot enter the stomach. Furthermore, the feedings and accumulated secretions in the blind upper segment enter into the trachea and death soon results from aspiration pneumonia. Reconstruction of esophageal continuity by a single-stage operation consisting of an extrapleural closure of the tracheoesophageal blind and an anastomosis of the esophageal segments offers the most satisfactory approach to the correction of the anomaly. A primary anastomosis of the upper and lower esophageal segments was done in 10 of the 21 patients for whom an exploration of the anomaly was undertaken. Six, or 37.5 per cent, of the 16 patients are living from seven months to three years and one month after the operation, and the reconstructed esophagus is patent in all instances.

The suspicion of a congenital obstruction of the esophagus is aroused by attacks of choking, dysphagia and cyanosis on attempts to swallow. The actual obstruction of the esophagus can be demonstrated by the inability to pass a catheter into the stomach. To be certain that the obstruction is complete iodized oil is given by mouth under fluoroscopic observation. A dilated blind upper esophageal segment, terminating usually at the level of the second or third dorsal vertebra, is then evident. The presence of a verified complete obstruction of the upper esophagus, the existence of air in the stomach is indicative of a communication between the esophageal segment and the trachea or a tracheoesophageal fistula. The absence of air in the stomach is not necessarily diagnostic of an absence of a tracheoesophageal fistula. The absence of a tracheoesophageal fistula can be determined also by fluoroscopic examination.

The diameter of the upper esophageal segment is always been of ample size to permit an anastomosis but the length may interfere considerably in the

performance of an anastomosis. If the upper segment is short and the lower segment reaches only to the tracheal bifurcation or to a main bronchus the difficulties are augmented. An unusually narrow diameter of the lower segment, a short length of the lower segment (agenesia) and a low position of the tracheoesophageal fistula were the important factors which prevented anastomosis in 6 of 7 patients.

Not bronchoscopy but exploratory operation offers the final criterion regarding the possibility of satisfactory reconstruction of the esophagus in those cases in which the presence of a tracheoesophageal fistula is evident because air is seen in the stomach.

The surgical problem is essentially a threefold one involving (1) the correction of the esophageal obstruction so that aspiration pneumonia will not occur, (2) the ligation of the tracheoesophageal fistula so that gastric contents cannot enter the trachea, and (3) the provision of some means for feeding the infant. Older methods have largely been supplanted by two plans that are now fairly well standardized insofar as surgical principle is concerned.

One plan, the indirect approach, consists of a three-stage procedure: (1) extrapleural ligation of the tracheoesophageal fistula, (2) exteriorization of the upper esophageal segment, and (3) gastrostomy. This indirect plan is essential for the maintenance of life if the anatomic conditions are such that a primary esophageal reconstruction is impossible.

The other plan, a direct approach to the problem advocated by the author, consists of a reconstruction of esophageal continuity by a single-stage extrapleural ligation of the tracheoesophageal fistula and a primary anastomosis of the esophageal segments. Feedings by mouth can be started soon after the operation. If leakage of the anastomosis does not result in an external esophageal fistula or a recurrence of a tracheoesophageal fistula, further operations are avoided.

The technical objection to the plan of primary anastomosis results from the fact that tension is invariably present at the site of the anastomosis. Tension occurs primarily because of the gap that often has to be overcome when the two segments are approximated. The weak tensile strength of the wall of the underdeveloped lower segment is a further technical disadvantage of the direct plan and makes advisable in all cases the complete relaxation that is obtained by general anesthesia, so as to permit the segments to be approximated as readily as possible.

Preoperatively the pulmonary status is carefully determined by physical and roentgenological examinations. If the infant is cyanotic, mucus should be aspirated from the pharynx and oxygen therapy should be started promptly. From the time that a diagnosis has been made, the patient is placed in the prone position with the foot of the bed elevated. This position favors the drainage of oral secretions to the exterior and lessens the tendency of aspiration of pharyngeal secretions. The position is changed to the alternate lateral positions at frequent

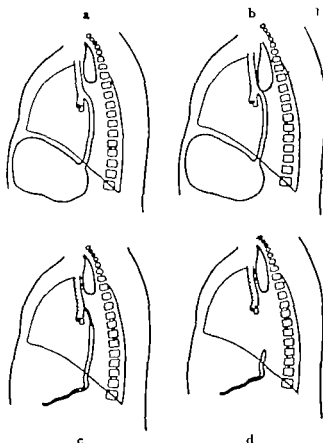


Fig. 1. The types of the anomaly that have been encountered at operation in 23 of the 24 cases upon which exploratory operation was performed are illustrated. (One patient died during operation before the nature of the lower segment was determined.) a, The most frequent type of malformation of the esophagus. The upper esophagus ends as a blind pouch. The lower esophagus arises from the trachea at a level that is usually between 0.5 and 1 cm. above the bifurcation of the trachea. Air is present in the stomach which indicates the presence of a tracheoesophageal fistula. This type of anomaly was present in 13 of the 24 patients upon whom a primary exploration of the anomaly was performed. Variations in the location of the fistula were found, and in 2 cases the lower esophagus arose from the right stem bronchus. The anomaly otherwise is the same as in a (5 cases). b, Partial muscular continuity of the two segments. The anomaly otherwise is the same as in a (5 cases). c, The lower segment is greatly contracted for a variable distance below its origin from the trachea and air has not entered the stomach, although a tracheoesophageal fistula was present (2 cases). In a third case, the lower segment was contracted, but air was present in the stomach (not illustrated). d, Atresia of the upper esophagus and agenesis of the lower esophagus. The stomach does not contain air (2 cases). (Courtesy of J. B. Lippincott Co.)

intervals to favor drainage from the upper lobes and thereby lessen the tendency for the development of an atelectasis of the upper lobes. Parenteral fluid consisting of a 3 or 5 per cent solution of dextrose in distilled water is given, preferably by the subcutaneous route. A blood transfusion is ordinarily not given before operation. Its use is deferred until the time of operation. Ascorbic acid and vitamin K are routinely employed as preoperative measures.

Ligation of the tracheoesophageal fistula and anastomosis of the esophageal segments can be performed through either a right or left extrapleural approach. In the 24 patients in the author's series for whom an exploration was carried out, the left extrapleural approach was used in 12 and the right extrapleural approach in 11. In the more recent cases in this series, the right extrapleural approach was used in preference to the left, because of the greater ease in obtaining the exposure of the lower esophageal segment.

The author describes the details of the operative technique using the right and the left approach, respectively.

The percentage of operative recoveries following anastomosis was 37.5. Pneumonia occurred in most of the fatal cases.

JOSEPH K. NADAR, M.D.

Adams, R. and Hoover, W. B.: The Management of Stricture of the Esophagus. *J. Thorac. Surg.* 1944, 3, 383.

The common disease conditions of the esophageal wall with obstruction are (1) cancer of the esophagus (2) esophageal diverticulum, (3) cardiospasm, (4) web (both with and without the Plummer Vinson syndrome) (5) cicatricial stricture secondary to caustic burns (6) cicatricial stricture secondary to peptic ulcer or esophagitis (often associated with peptic ulcer below the esophagus) (7) cicatricial stricture secondary to tuberculous glands of the mediastinum, and (8) congenital developmental anomalies. They have been named in the order of greatest frequency.

The method of treatment of esophageal strictures is dilatation of the narrowed area. A satisfactory result is obtained when the dilatation is sufficient to allow the passage of a regular diet without difficulty. Until this is accomplished the diet may be altered to admit its passage through the narrowed esophagus.

The amount of dilatation or distention that may be obtained in tissues by the application of pressure is to say the least, amazing. In the esophagus may be seen diverticula that have become as large as a grapefruit, and the esophagus may attain a circumference of 10 inches as the result of continued pressure from its fluid content, and the added pressure exerted by the muscles of deglutition.

Passage of the instrument through the esophagus is fraught with danger for trauma to the esophageal wall may result in mediastinitis while perforation or rupture produces mediastinitis except in rare instances. The mediastinitis spreads rapidly and terminates fatally in almost all instances unless radical measures are taken to drain the infection and limit its spread. In such cases the judicious use of the sulfonamides and penicillin must not be overlooked.

The authors review their experiences in the procedure of dilatation of the esophagus for some of the conditions mentioned. They stress particularly the problems they encountered. They have found that it helps a great deal to pass a thread either above or below (in all cases in which this is possible) when

dilatation is attempted, or when the esophagography or bougies are used.

PAUL MICHAEL, M.D.

Ferrari, R. C. and Iturraspe, M. C.: Megaesophagus. Esophagogastrostomy by the Thoracic Route (Megaeosofago. esofagogastronomia por via toracica). *Rev. Acad. argent. cir.* 1944, 18, 509.

Megaesophagus may be treated by dilatation or by operation. The authors describe in detail 7 cases that they operated on and refer to 2 others operated on by colleagues. In all of these successful results were obtained.

The first patient was a farmer forty five years of age who began to have difficulty in swallowing solid foods in 1940 and then for six months the difficulty had extended to swallowing liquids. He had lost 19 kgm. in weight. In January 1943 he was hospitalized with a diagnosis of cancer of the cardia. On operation the cardia was found hard and fibrotic with no palpable glands. A Witzel gastrostomy was performed, but without success and he was sent to the authors for treatment. Roentgen examination showed the dilated esophagus to be filled with retained fluid; it also showed a megacystic mold. This was the second case of this type that the authors have seen. The ninth rib was resected for a length of 18 cm. 3 cm. of the eighth rib were resected at the posterior angle. The pleura was opened and the phrenic nerve was sectioned over the pericardium. A radiating section of the diaphragm was made about 10 cm. from the esophageal opening. The rigid cardia was adherent to the esophageal opening, these adhesions were cut. The esophagus above the cardia was enlarged to about twice its normal size. A lateral anastomosis not involving the cardia was performed between the esophagus and the body of the stomach. Because of the relation of the cardia to the esophageal opening operation by the abdominal route would have been impossible. Recovery was normal and the results were good. The patient can swallow normally and there is no regurgitation. A supplementary operation was performed on the sigmoid sphincter to relieve the stubborn constipation from which he suffered.

The second patient was an Italian fifty-three years of age in whom a Witzel gastrostomy and dilatation were performed before esophagogastrostomy was decided on. The gastrostomy was done under local anesthesia and the final operation under cyclopropane-ether given by tracheal intubation, just like in the first case. Recovery was uneventful, and the functional result was good in this case also.

The discussion was devoted to the relative merits of the thoracic and abdominal routes in this operation, with general agreement that the thoracic route is to be preferred when the surgeon is skilled and the operation is performed in a hospital where all necessary apparatus is available.

In closing, the author said that these were two different operations. In the abdominal operation the esophageal opening is dilated to bring down the esophagus to the stomach, but the pillars of the

diaphragm remain intact and function of the diaphragm is preserved. However in the thoracic operation the diaphragm is paralyzed by section of the phrenic nerve and radiating incisions are made in the diaphragm. These destroy the esophageal opening, and a true hernia of the stomach through the diaphragm is brought about. This cannot have any action on the anastomosis and naturally the results of this operation are better.

AUDREY G. MORGAN M.D.

Harrington S. W. and Moersch, H. J.: Surgical Treatment and Clinical Manifestations of Benign Tumors of the Esophagus, with a Report of 7 Cases. *J Thorac Surg* 1944, 13: 394.

The occurrence of benign tumors of the esophagus is relatively infrequent. Their subjective symptoms and clinical manifestations are often meager which not only delays their clinical recognition but also makes it difficult. These growths are potentially malignant and their treatment is of special interest to the surgeon because extensive operative procedures may be required for their removal.

These benign tumors may be divided into two main groups: the mucosal and the extramucosal tumors. The mucosal tumors are often pedunculated and arise from the submucosa. They usually are fibroidipomas or fibromyxomas and are covered by normal epithelium of the esophagus. The extramucosal, or intramural, tumors arise from the muscle of the wall of the esophagus; they do not involve the mucosa and usually are leiomyomas.

The growth of benign tumors of the esophagus is usually slow and the tumors may attain considerable size without giving rise to subjective symptoms. This is true particularly of the intramural tumors, which rarely produce obstruction of the esophagus unless they attain great size. The common symptoms associated with these growths are dysphagia, substernal pain, regurgitation of food, cough, and dyspnea. The pedunculated tumors are commonly associated with obstructive symptoms and the diagnosis of these growths is often definitely established by regurgitation of the tumor into the mouth, which may be the first subjective symptom. Regurgitation of these growths into the nasopharynx can imperil life because of their blocking the trachea which may result in strangulation.

The roentgenographic and roentgenoscopic examination of the esophagus is of great value in determining the presence of these growths. Esophagoscopy examination is of utmost importance in establishing a definite diagnosis although at times it may be difficult to determine the site of origin as well as the type of growth because it is difficult to obtain a specimen for biopsy through the normal esophageal mucosa. The site of origin of the pedunculated tumors usually can be determined definitely.

The indications for surgical treatment of benign tumors are not as urgent or as imperative as for malignant lesions of the esophagus. They depend somewhat on the patient's general condition the

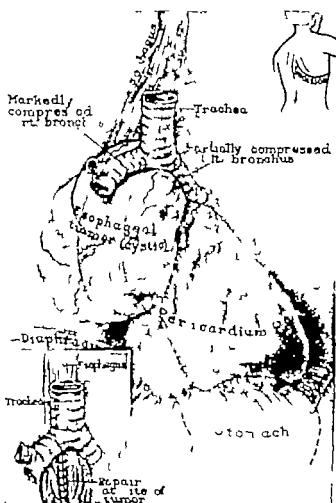


Fig. 1. Cystic tumor originating from the anterior wall of the middle third of the esophagus, displacing the esophagus to the right (and posteriorly) causing marked compression of the right main bronchus, moderate compression of the left main bronchus, and widening of the coronary angle. Tumor is adherent to the right portion of the pericardium. Upper right insert shows posterolateral incision for transpleural removal of the tumor. Left lower insert shows repair of the esophagus at the site of the tumor.

amount of difficulty the tumor is causing, and the site of the tumor. Inasmuch as these growths may undergo malignant change, surgical treatment should be considered in all cases.

The surgical treatment of these tumors depends on whether the growth is submucous or pedunculated, or on whether it arises from the outer portion of the muscular coat of the esophagus. The pedunculated tumors may be more accessible and amenable to surgical treatment than the intramural tumors. If the pedunculated tumor is small and its origin is high at the introitus it may be removed through the mouth with a snare and cautery. Larger tumors of this type require cervical esophagotomy. These tumors may attain such huge size as to require transthoracic esophagotomy. This approach also may be necessary if the pedicle of the tumor is situated low in the esophagus.

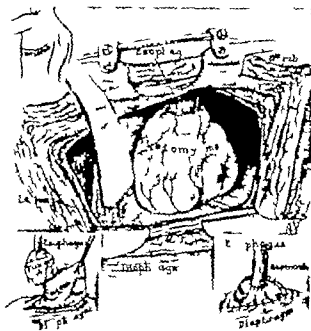


Fig. 2. Resection of the lower fourth of esophagus for removal of a leiomyoma. The stomach was transposed into the thoracic cavity (lower left insert) and the esophagus was anastomosed to the anterior wall of the stomach (lower right insert).

The indications for surgical treatment of intramural tumors are not, as a rule, as urgent as those for pedunculated tumors because intramural tumors do not usually cause obstructive symptoms. The surgical treatment of these tumors often requires a much more extensive operative procedure than is necessary in cases of pedunculated tumors. If the intramural tumors involve only a segment of the wall of the esophagus they may be removed by local excision of the tumor from the wall of the esophagus which is then reconstructed. If the growth involves the entire esophageal wall, its removal will require resection of the esophagus, which entails a greater operative risk.

In 5 of the 7 cases which the authors report esophagectomy was performed in 1 case resection of the esophagus was done and in 1 case the tumor was removed orally with a snare and cautery.

MISCELLANEOUS

D. Abreu, A. L. Litchfield, J. W. and Hodson, C. J.: Intrathoracic Metallic Foreign Bodies. *Lancet* Lond. 1944 547 865.

In a series of 564 severe chest casualties 93 had retained intrathoracic missiles. In 30 cases operative removal was thought necessary and in 49 of these the missile was found and removed. Operative removal of foreign bodies 1 cm. or more in diameter is attempted in view of the risk of infection hemorrhage and structural damage. Operation for the

removal of missiles is delayed until the abnormal physiology due to the injury is overcome. On the other hand too long a delay is not advisable because dense adhesions may form. The foreign body must be accurately localized by x-rays and fluoroscope. If the missile is not easily found at operation portable films should be taken.

A total of 23 patients had missiles removed from the lung in all but 1 the foreign body was a shell fragment. In 5 cases infection was recent, adhesions and palpable tracks leading to the missile were found frequently. Occasionally cavities were present about the metal. In 3 cases calcified nodes near the fragment made identification difficult. In only one case was a lobectomy necessary.

Fourteen cases of pleural foreign bodies were subjected to operation. They offered no special problems when properly localized. Two peripheral and 3 mediastinal fragments were removed. Three missiles were localized in the heart. In 1 of the cases the missiles were not causing symptoms and exposure was not done. In the third case exploration was done but the foreign body was found to be in the interventricular septum and could not be removed. The patient died as did 1 of the patients who had a missile removed from the lung. These were the only operative deaths. THOMAS F. THOMAS, JR., M.D.

Lorena, R.: Radioactivity and Lung Cancer: A Critical Review of Lung Cancer in the Mines of Schneeberg and Joachimsthal. *J. Nat. Cancer Inst.* 344 5 2.

Because of the growing conviction in the United States and abroad that radon gases emitted by rocks inhaled for long periods of time or emitted from radioactive deposits in the lungs will cause cancer of lung in man, the author, Mr. Egro Lorena (a senior biophysicist of the National Cancer Institute of the United States Public Health Service) has presented this review of the literature on pulmonary cancer in the miners of Schneeberg and Joachimsthal. The conviction is based on the fact that primary carcinoma of the lung accounts for 30 per cent of the causes of death of the miners of Schneeberg and Joachimsthal. These mines contain radon, especially where pitch blend is mined. With the use of ever increasing amounts of radon in industries, it is important to know whether radon from radioactive substances will induce pulmonary cancer. Schneeberg is in Germany and Joachimsthal is in Czechoslovakia. The author gives a brief history of the mining activities of these two regions. In addition, he stresses the living, working, and social conditions of the two areas. The article quotes the findings of a great number of men who have studied and obtained material both from the histories and autopsies of individuals in the two regions. Hartung and Hesse reported findings as early as 1879. They found that in 75 per cent of all deaths the cause was lung cancer and that the incidence was greater in miners than in masons or carpenters working in the mines in 1911. Arnsperg reported statistical data showing

that from 1875 to 1912 276 miners had died of cancer of the lung, 64 of tuberculosis 119 of other lung diseases, and 206 from other causes. He was the first to diagnose the cancer as squamous-cell carcinoma. Uhlig in 1921 and Beyreuther in 1924 described isolated cases of lung cancer. Others who have reported include Rostoski and Saupe, Ludwig Lorenser and many others.

The author in reviewing the literature from the many who have reported, has attempted to correlate the histories, the autopsy findings and the living conditions under which these miners work. He then quotes literature giving the radium content of the minerals present, also the radon content of the area in the mines. After this, animal experiments with the animals under conditions similar to those in the mines were made. The animals used included rats, mice and rabbits. The author gives the conditions under which the animals were studied, the amount of exposure to radon, and then the necropsy findings.

In summarizing the findings he states we find that large doses of x or y rays to the lungs (doses in which the total absorbed energy was above 10^4 ergs per cc. of tissue) have not produced lung tumors. Therefore it seems unlikely that the miners of Schneeberg and Joachimsthal exposed daily to the concentration of radon of 3×10^{-3} curies per liter for twenty years should develop lung cancer as the total energy absorbed during that time per cubic centimeter of lung tissue amounts to only approximately 1×10^3 ergs. The energy absorbed in the lungs of the mice of Read and Blottram during 161

days was of the same order of magnitude. No lung lesions were found in these mice. Certain strains of mice have a high susceptibility to spontaneous lung tumors and others a low one but generally the statement of Slye, Holmes, and Wells holds. It seems that man exhibits lung tumors exceptionally infrequently and that mice show an even more exceptional prevalence of tumors of this organ. Evans states "It will be noted from these data that rats and mice are about 40 times as resistive as humans to lesions caused by a rays when all dosages are expressed in erg units. The extrapolation of the results of animal experiments to man must recognize this great difference in susceptibility."

This statement seems not to be justified as far as the effect of radon on lung tissue is concerned.

Therefore, the opinion that radon is the sole cause of the lung cancer of the miners cannot be maintained. The contributing factors in the case of the miners which were already brought up in the different investigations discussed may include the following: pneumoconiosis produced by the dust in the mines; chronic irritation caused by respiratory diseases; arsenic, radioactive substances, and perhaps a hereditary susceptibility. The mines have been operated for hundreds of years. As frequently is the case in Europe the occupation of the father is taken over by the son, the miners live in isolated places and inbreeding often occurs. All these factors may lead to a hereditary susceptibility. However no statistical evidence on this point has ever been collected.

PAUL MERRILL, M.D.

SURGERY OF THE ABDOMEN

ABDOMINAL WALL AND PERITONEUM

Sidel, N. and Wolbarsht, A.: Spontaneous Pneumoperitoneum from an Unknown Cause. *N England J M* 1944, 33: 450.

Pneumoperitoneum may be a spontaneous, diagnostic, or therapeutic condition. When it is encountered except in the form induced for diagnosis, there is usually some lesion in the gastrointestinal tract as the causative factor. Perforation of a viscus is the usual cause. In some cases, the perforation is a slowly developing leak rather than a sudden puncture.

A case of spontaneous pneumoperitoneum, without demonstrable cause and without symptoms is reported. The pneumoperitoneum was discovered accidentally during the course of pneumonia. Subsequently the condition spontaneously disappeared. No gastrointestinal abnormality was found in the history, laboratory tests, or on x-ray investigation. There was x-ray evidence of the marked pneumoperitoneum and of its complete disappearance after a three month interval. SAMUEL KAMEN, M.D.

GASTROINTESTINAL TRACT

Colp, R., Kligenstein, P., Maga, S. and Drucker, L. J.: Subtotal Gastrectomy for Duodenal Ulcer. *Ann. Surg.* 1944, 20: 70.

For six years a definite program has been followed on patients suffering from peptic ulcer. Under this program 173 cases were treated with special emphasis on preoperative management, anesthesia, operative technique, and postoperative care.

Statistics are presented in table form showing the duration of the disease. The important facts in history, analysis of age and sex, choice of operation, pathology, type of gastrointestinal anastomosis and an analysis of pertinent data as to deaths are given.

Gastric analysis showed a uniformly high acid gastric content. Gastroscopic examinations were of no direct value in cases of duodenal ulcer. A high protein diet was used to combat hypoproteinemias. Inhalation anesthesia used during the first three years gave way to continuous spinal anesthesia.

Retrocolic gastrojejunostomy has in turn been replaced by an antecolic isoperistaltic anastomosis. Jejunostomy was used as a complementary or supplementary procedure when indicated. A lower mortality in the second group was attributed in part to spinal anesthesia, the wider use of drainage of the duodenum in the antecolic type of anastomosis, and the frequent use of jejunostomy for alimentation.

The high mortality resulting from early operations on bleeding ulcers will be combated in the future by allowing the patients to convalesce to a nearly normal state before radical surgery is attempted.

RICHARD J. BICK, M.D.

Bremer, J. L.: Diverticula and Duplications of the Intestinal Tract. *Arch. Path., Chic.*, 1944, 31: 17.

The group of anomalies comprising the microgastroschisis, intestinal duplications, and the hirsutic diverticula are divisible into two smaller classes on the basis of embryologic origin. Most of the spherical cysts are derived from true diverticula, which are frequently found projecting from the ventral or antimesenteric surface of the tube in embryos of the eighth or ninth week, and are normally absorbed later. Abnormally they continue to grow. If restricted by the intestinal muscle they bulge within the lumen, but if they pierce the muscle layers outward expansion is unlimited and they may become large cysts attached to the intestine. Their wall is necessarily thicker than the gut wall.

A few of the spherical and most of the tubular structures represent true duplications, which originate by an abnormal persistence of the vacuoles normally present among the mesodermal cells of the solid stage of the intestine. A phenomenon of growth in embryos of the sixth or seventh week. By the confluence of a chain of vacuoles a new channel is formed parallel to the original lumen, and the channel becomes separated from the latter by a union of the intestinal layers between the two. Since the duplication develops within the intestine, the outer wall of the duplicate portion always contains all of the tissue layers of the intestine. The duplicate lumen usually lies between the leaves of the mesentery, but may be entirely separated, with a mesentery derived by the splitting of the original. It may open into the main lumen at one or more places, or become a closed cyst. Theoretically three or more channels are possible, the main lumen and two or more confluent chains of vacuoles.

The duplicate structures assume many forms, some of which are shown and described, and are often associated with other anomalies. In the tubular portions the mucosa tends to resemble that of the parent tube, but in bulbous or cystic portions it changes to the gastric type. Great internal pressure may destroy mucosa of any type.

JOHN E. KIRKPATRICK, M.D.

Kaufman, L. R. and Helman, H. I.: A Case of Spontaneous Gastrojejunal Fistula Eight Years after an Operative Gastrojejunostomy. *Surg.* 1944, 16: 557.

A spontaneous gastrojejunal fistula occurring eight years after an operative gastrojejunostomy is unique. There is no similar case recorded in the literature, nor has one ever been reported by any other physician.

A seventy-year-old white woman was admitted to the Metropolitan Hospital, New York, on April 1, 1943 on account of dysphagia, nausea, and the loss of 10 pounds in three months. She had had dyspepsia

and nausea since youth. A posterior gastroduodenostomy for duodenal ulcer made her comfortable and symptom free for the first time in her life. The patient appeared chronically ill, showed evidence of loss of weight and a marked pallor.

On x-ray examination and fluoroscopy, a normal esophagus was found, the stomach was enlarged and contained a five hour residue, but no gastroduodenal stoma was visualized.

Gastric analyses revealed high total acid up to 75, high free acid up to 48, and high combined acid of 27; there was occult blood in the majority of the specimens.

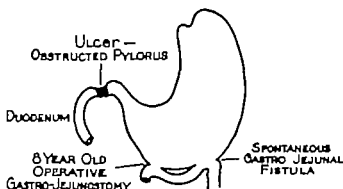
Gastroscopy revealed a patchy superficial gastritis, an adherent exudate, punctate hemorrhages, atrophic rugae, and a pseudovalve of the stoma with an opening large enough for easy and clear visualization of the jejunum. Many peristaltic waves indicated possible obstruction below the stoma. 2,000 cc of gastric residue were found.

The treatment consisted of gastric lavages, transfusions, and the administration of liver and iron. The hemoglobin increased from 53 to 70 per cent with marked subjective and objective improvement.

Exploratory laparotomy was undertaken after three weeks with the intention of performing a subtotal gastrectomy. The stomach was greatly dilated. Adhesions of the anterior surface to the round ligament and to the parietal peritoneum were easily separated. An anastomosis was visualized at the usual gastroduodenostomy site; there were sharp angulations of proximal and distal jejunal loops. The apparent stoma was located in the transverse mesocolon at the edge of the colon in a large inflammatory mass about 11 by 4 by 7 cm. This mass was dissected from the colon and mesocolon and then from the stomach. The jejunum attached to this mass was resected and an end-to-end anastomosis was made. The gastric wall was inflamed and thickened for a radius of about 2 cm. around the anastomotic site. That portion of the wall was resected. Finger exploration through this opening revealed that distal to it was a wide orifice into what was thought to be the duodenum. However, autopsy showed this orifice to be the original gastroduodenostomy. The anastomosis was the spontaneous inflammatory gastroduodenostomy. The defect of the stomach wall was completely closed and the rent in the mesocolon was sutured. While the stomach was open a Levin tube was guided well into the small intestine.

In the postoperative period oxygen and several transfusions were given. The Levin tube was aspirated at intervals and large quantities of dark brown fluid were removed. Twenty-four hours after operation the patient suddenly went into shock and expired.

At autopsy the gastric mucosa was found to be reddened but not ulcerated. Rugae were not prominent. The pyloric region showed complete obstruction with an area of white scar tissue occluding the opening into the duodenum. An apparently well functioning anastomosis was present. Proximal to



this anastomosis was a sutured defect of the posterior gastric wall. In the descending loop of the jejunum distal to the gastroduodenostomy was an end-to-end anastomosis surrounded by some edema. The mesocolon was scarred and the transverse colon was thickened.

No new gastroduodenostomy was performed since the pylorus and the duodenum were assumed to be patent. Autopsy however showed that there was complete obstruction and that the old gastroduodenostomy was functioning normally.

The most discussed complication following this operation is gastroduodenal ulcer. Fistulas when present, generally are gastroduodenal, jejunojejunal, and gastroduodenocolic. High acid values obviously cause recurrent ulcers, especially when the pylorus is closed. Most gastroduodenal ulcers are clinically similar to peptic ulcers.

The authors quote Alvarez: "Anything that interferes with the passage of duodenal contents over the jejunal mucosa around the stoma is likely to leave this region unprotected from the corrosive effects of gastric juice and, therefore, subject to ulceration. Closure of the pylorus probably interferes with the maintenance of a good downward current in the duodenum, and the absence of food and gastric juice in the duodenum lessens the outflow of the protective bile and pancreatic juice." They also quote Lahey:

"Pyloric obstruction is a predisposing factor for gastroduodenal ulcer since the highly acid gastric contents are dumped into the jejunum and cannot mix with the regurgitant alkaline contents."

Evaluating the pathology in this case the authors assume two hypotheses: (1) the ulcer may have originated in the greater curvature of the stomach as a new ulcer, or (2) the ulcer may have developed as a jejunal ulcer about 8 cm. distal to the original gastroduodenostomy in a location where the impact of the acid chyme would be most likely to produce mucosal ulceration.

As the ulceration progressed through the serosa inflammatory reaction could readily fix a distal segment of the original loop to the greater curvature as well as to the gastroduodenal omentum since it was in close proximity to both. The resulting perforation is then readily understood.

MATTHIAS J. SKIFFERT, M.D.

Dixon C. F. and Benson R. E.: Closure of a Colonic Stoma. Improved Results with Combined Succinylsulfathiazole and Sulfathiazole Therapy *Ann. Surg.* 1944, 120 568.

The oral administration of succinylsulfathiazole and the local application of sulfathiazole to the oper-

ative wound following closure of a colonic stoma have greatly improved the results obtained by the authors. Infection of the operative wound occurred in 84 per cent, and a fecal fistula developed in 30 per cent of a series of 102 cases in which sulfonamide drug was employed, whereas infection of the wounds occurred in only 13 per cent, and a fecal fistula occurred in only 2 per cent of 102 cases in which a combination of succinylsulfathiazole and sulfathiazole was administered. These improvements in the results are in a large part attributable to the new chemotherapeutic agent succinylsulfathiazole, and they indicate in general the usefulness of the drug in the management of surgical diseases of the lower intestinal tract.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Shallow T. A., Eger S. A., and Wagner F. R.: The Conservative Management of Acute Pancreatitis. *Pennsylvania M. J.* 1944, 47 199.

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No one of the current theories adequately explains the mechanism of the production of the disease. There is autodigestion of the pancreas by its own secretion but how the enzymes become activated is not well understood. The liberation of trypsin leads to digestion of the pancreas with necrosis, sometimes followed by suppuration. The tryptic digestion of blood vessels within the gland results in hemorrhage. The liberation of lipase is responsible for an important feature of the disease, namely, fat necrosis. Absorption of the split protein products of the trypsin itself may account for the development of profound shock and death in the very severe cases.

There are two distinct pathological types of the disease: the common form and fortunately the milder acute interstitial pancreatitis or acute pancreas edema. In this condition the gland is grossly enlarged and hard and is surrounded by small areas of fat necrosis localized to the pancreas. Subsequently the inflammation is accompanied by fibrosis. In the less common form, namely the hemorrhagic type, there is blood tinged fluid in the lesser peritoneal cavity. Some of this may find its way into the general peritoneal cavity. The pancreas grossly enlarged, soft and friable and it may be black and

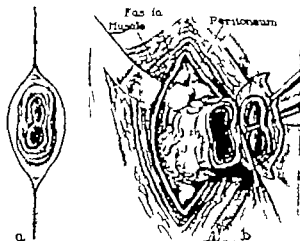


Fig. 1. Closure of colonic stoma. a, Incision in skin encircling the stoma. b, The fascial, muscular and peritoneal layers have been incised and the proximal and distal limbs of the colon are mobilized. The previously encircled layer of skin and subcutaneous tissue is being excised from the wall of the bowel. The edges of the colonic stoma are freshened. (Courtesy of J. B. Lippincott Co.)

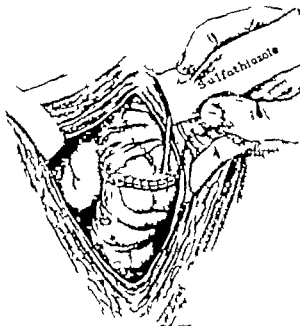


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EAL O LATIMER M.D.

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CHARLES BARON M.D.

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Presented at the Twentieth Lewis and Clark Lecture of the Frank Billings Foundation the author gives the results of investigations that have been under way in the Gastrointestinal Clinic at the University of Pennsylvania Hospital Philadelphia for the past ten years. They have grown out of a tech-

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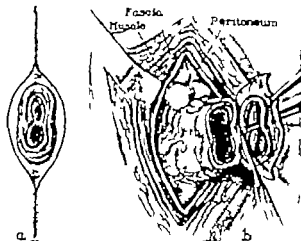


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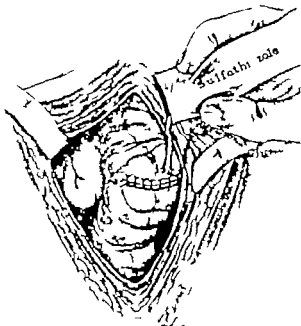


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EARL O. LAMMER, M.D.

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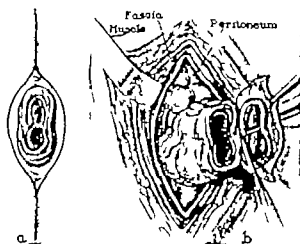


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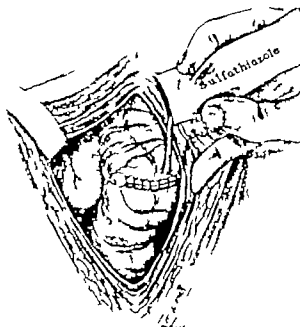


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6. The transverse mesocolon is repaired except in the region below the pylorus. Here, one or two soft rubber drains are inserted to the site of pancreatic transection.

7. Closure of the abdominal wound.

In some instances of redundant stomach, the gastrophrenic omentum may be transected, the stomach retracted downward and the body of the pancreas excised over the lesser curvature of the stomach.

Total duodenopancreatectomy and splenectomy for practically complete replacement of the pancreas by carcinoma was performed in 2 patients.

CHARLES BARON, M.D.

MISCELLANEOUS

Miller, T. G.: Intubation Studies of the Human Small Intestine. A Review of a Ten Year Experience. *Gastroenterology* 1944, 3 131

Presented as the Twentieth Lewis Linn McArthur Lecture of the Frank Billings Foundation, the author gives the results of investigations that have been under way in the Gastrointestinal Clinic at the University of Pennsylvania Hospital, Philadelphia, for the past ten years. They have grown out of a tech-

nique for intubation of the small intestine and, more or less by chance, have led to a procedure of some practical importance in the management of patients with intestinal obstruction.

The technique of intubation permits many investigations of the function of the small intestine including certain physical and chemical facts regarding the fasting contents at various levels and the influence of certain factors on the characteristics of the fasting contents. For preliminary studies the tube was introduced when the subject was in a fasting state.

Fasting specimens obtained by 51 intubations in 30 normal subjects showed that the rate of flow of the contents averaged less than 1 cc. per minute; that the reaction, though usually acid in the duodenum and sometimes so in the jejunum, was essentially neutral throughout the ileum; and that the osmotic pressure, though lower in the duodenum, tended in the jejunum and ileum to be the same as that of the blood plasma (approximately 300 millimoles).

These conditions are altered when solutions are orally administered before the intestinal collections are made because of gastrointestinal motility.

The influence of the ingestion of glucose and food was also studied, as well as the condition in isolated segments.

As glucose enters the gut a normal osmotic pressure is maintained by (1) a displacement of the chloride and bicarbonate ions; (2) an inflow of hypotonic fluid; (3) dispersion of the contents; and (4) absorption of the glucose.

For the preservation of normal conditions above the bowel after the admission of a hypertonic solution, nature employs at least one other procedure in outpouring of mucus that acts as a blanketing layer between the mucosa and the irritant material.

From the beginning the Miller Abbott tube is used in the development of a satisfactory technique for the study of absorption from the intestine.

By special methods the author has been able to make some very preliminary studies on proteolytic digestion, as well as to study the effects of drugs on intestinal functions.

In intestinal obstruction, the chief merit of the two-lumened apparatus lies in the fact that it reaches the point of obstruction and so acts as an internal enterostomy or in the case of an adynamic ileus, as a deflator of the entire bowel. Wengertsen himself admits that his technique has two disadvantages: i. e. the tube does not reach the site of the lesion, and it does not permit use of the bowel above the lesion for purposes of nutrition. Both objections are overcome by intestinal intubation.

In addition to its principal actions—decompressing the distended intestine, aiding in the correction of fluid and electrolyte imbalance, converting emergency cases of obstruction to an elective surgical status, and rendering subsequent operation less hazardous—intestinal intubation also may be an aid in diagnosis. Not infrequently it is capable of localizing the site of an obstructive lesion and by permitting the injection of a thin barium mixture at that point, it may give information as to its nature.

HARRY W. FUNK, M.D.

GYNECOLOGY

UTERUS

Viergliver E. and Pommerenke, W. T.: Measurement of the Cyclic Variations in the Quantity of Cervical Mucus and Its Correlation with the Basal Temperature. *Am J Obst* 1944 48 351

The authors desired to measure accurately the amount of mucus in the cervix at various times in the menstrual cycle by using the basal body temperature shift as the method for fixing the time of ovulation.

The mucus from the cervical canal was withdrawn by aspiration with a glass cannula of known weight. The cannula was then weighed with the mucus and the difference in weight determined the amount of secretion.

Daily vaginal temperatures on arising were taken and recorded.

The study was carried out on 4 subjects in the first subject through six consecutive cycles in the second through three nonconsecutive cycles in the third for one cycle and in the fourth through three consecutive cycles.

A total of 151 observations were made. In the group as a whole, the amount of mucus was increased from about the eighth through the eighteenth day. The individual peaks varied. The usual amount of mucus found preceding or following the days of increased secretion was about 60 mgm. During the periods of increased secretion the amount varied from 200 to 400 mgm. The viscosity of the mucus was usually low from the eighth through the sixteenth day. The maximum secretion of mucus preceded the temperature rise by at least one day.

The authors believe that this may be explanation of the fact that some individuals failed to be come pregnant having had coitus after the temperature rise.

HENRY C. FALK, M.D.

Karnaky A. J. The Use of Diethylstilbestrol to Control Uterine Bleeding. *Southern J* 1944 37 510.

The author attributes normal menstruation and dysfunctional uterine bleeding to fluctuations in the blood estrogenic level. If the estrogenic level is above or below certain limits amenorrhea occurs. On the other hand, if the level is elevated into the bleeding range or if the higher estrogenic levels are lowered into the bleeding range, endometrial bleeding will occur. The degree and rhythm of uterine bleeding will depend upon intrinsic factors which influence the elevation and lowering of the blood estrogenic levels. These factors are dependent upon the metabolism of the granulosa cells.

The author states that all types of dysfunctional bleeding, even if due to fibromyomas as well as amenorrhea may be controlled by the use of large enough doses of stilbestrol.

Four hundred consecutive patients with multiple myomas which were associated with uterine bleeding were given from 50 to 250 mgm. of stilbestrol daily for from ten to sixty days. In all except 8 cases the bleeding stopped.

The method of treatment is as follows:

If the bleeding is severe from 10 to 50 mgm. of stilbestrol are injected into the cervix, or given by mouth every fifteen minutes until the bleeding stops which usually occurs in from two to twenty four hours. Following this from 50 to 100 mgm. are given by mouth each night for a period of from thirty to forty nights. Combined with the stilbestrol thyroid and lipodine are also given.

The author attributes the action of stilbestrol in the control of bleeding to inhibition of the gonadotropic hormones of the pituitary gland plus a diminution in tone of the uterine musculature which is thought to be the result of increased vasodilatation in that area. The increased vasodilatation is followed by an absorption of irritating metabolites with a resultant lessening of the irritation of the smooth muscle.

Among a series of 327 cases 89 per cent of the patients were able to continue the use of large doses of stilbestrol with only a transient period of nausea. The remaining 11 per cent were given elixir of phenobarbital to control a more pronounced gastrointestinal disturbance. In only 0.15 per cent was it necessary to stop stilbestrol because of gastrointestinal symptoms. The administration of large doses of vitamin C (800 mgm. daily) is said to reduce the incidence of nausea. No untoward physical effects were noted from the large doses of stilbestrol.

J. ROBERT WILLSON, M.D.

Ayre, J. E.: A Simple Office Test for the Diagnosis of Uterine Cancer. *Canad M J* 1944 51 17.

In 1941 Papanicolaou and Traut presented an office procedure for the early diagnosis of uterine cancer. This method employed the vaginal-smear technique.

Ayre presents a simple modification of this technique to make the test more rapid and more effective. This modification consists in taking the smear directly from the external os of the cervix. Here the concentration of cancer cells is greater. This was found to be the case in the series of cases studied. Although cancer cells may be found in the vaginal smear the diagnosis should be confirmed by biopsy before operation or radiotherapy. The test is simple and rapid. The biopsy can be taken by any physician and sent to a laboratory for skilled interpretation. Every woman manifesting spotting of blood should have the benefit of a vaginal smear and any positive or doubtful case should have a biopsy without delay.

The technique is presented together with 2 cases illustrating the use of the smear diagnosis.

T. FLOYD BELL, M.D.

ADnexAL AND PERIUTERINE CONDITIONS

MacClure E. Olavo J and Oliveira, C.: Hydatidiform Mole of the Ovary (Mola hidatiforme do ovário) *An. bras. gine* 1944, 8 94.

The interest of the case presented lies in the fact that hydatidiform mole of the ovary is extremely rare. Novak found only 3 cases which had been reported.

The patient was a woman of twenty-one years who was admitted to the hospital with a diagnosis of ruptured ectopic pregnancy on the left side. A week before she had had intense abdominal pain followed by signs of internal hemorrhage. She was operated on immediately after admission. The uterus was found to be congested, the tubes were intact. The left ovary was ruptured and tissue resembling that found in the placenta protruded from the opening. This had been the source of the hemorrhage. A cuneiform resection of the ovary was performed and the wound closed. Uneventful recovery took place and the patient was discharged from the hospital on the eighth day.

Histological examination showed the typical picture of hydatidiform mole localized entirely in the ovary. The later course and the demonstration of negative Aschheim-Zondek tests at the end of three and five months after the operation showed that the condition was benign. Photomicrographs of the findings are given in the original article.

AUDREY G. MORGAN, M.D.

EXTERNAL GENITALIA

Hass, R. L.: Genital Tuberculosis in the Female. *Am. J. Obst.*, 1944, 48 69.

This study is based on a series of 62 cases seen over a period of twenty years. The patients ranged in age from fifteen to sixty-one years. Sixty per cent of the patients were between twenty and forty years of age when admitted.

The chief complaints which brought the patients to the hospital were abdominal pain in 35 per cent of the cases, sinuses or fistulas in 16 per cent, vaginal bleeding in 11.3 per cent and back pain in 11.3 per cent. All other complaints formed less than 5 per cent of the cases.

Although vaginal bleeding was the complaint in only 11.3 per cent of the cases, 58 per cent of the patients in the series complained of some change in the menstrual cycle. This was to be expected since

the endometrium and ovaries were frequently involved.

Sterility occurred fairly frequently in this series. Forty-six patients were married and in the child-bearing age. Twenty of these had not been pregnant making the incidence of "infertility" 43.5 per cent. Forty-eight per cent of the patients had other active foci in addition to the genital lesion.

Eight patients in the series received nonoperative treatment. Four of this group had far advanced generalized tuberculosis and died on an average of three and six tenths months after admission. Three were treated by bed rest, adequate diet, and ultraviolet light, and 2 were alive and well after ten and one years respectively. The third patient in this group died within eight months after admission. One patient with tuberculosis of the cervix refused treatment and is alive twenty years after being seen. She denies any symptoms except amenorrhea at the present time.

Fifty-four patients were treated surgically, the abdominal cavity being opened in 39.

Complete pelvic exenteration with total hysterectomy and bilateral salpingo-oophorectomy was done in 13 cases. In 13 additional cases the same treatment as in the first 13 was given except that the cervix was not removed. In the remaining 23 cases all other operations, including vaginal hysterectomy, removal of cysts, posterior colpotomy and drainage of abscesses, were done.

In this series there were fistulas or wound infections in 24 per cent. In the last 10 patients operated upon since 1936 there have been no wound complications.

The primary operative mortality was 5.5 per cent. Two patients died on the fourth postoperative day, one of pulmonary embolism and the other of peritonitis and intestinal obstruction. A third patient died on the nineteenth day of generalized tuberculosis.

All 62 patients in this series have been carefully followed up. Seventeen (25.8 per cent) are dead after an average of two and three-tenths years. Five died of causes related to pelvic tuberculosis or its extension. The remaining 12 died of causes other than pelvic, the most common being pulmonary and generalized tuberculosis.

Forty-five patients (74.2 per cent) are alive, an average of ten and one half years after their original admittance. Over half of these (57.7 per cent) claim good health. Wound sinuses persist in only 3 patients.

HENRY C. FALK, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Hughes T. D.: Syphilis in Pregnant Women. A Study Based on the Routine Wassermann and Kahn Tests Performed on 28 924 Patients. *Med. J. Australia* 1944, 2: 273

This examination of the blood for syphilis by means of the Wassermann test was commenced by the author in March, 1943 and the figures are carried forward to December 1943. In all 28 924 patients have now been tested and 160 were found to give a positive reaction which was checked in all of the cases. This gives an incidence of 0.55 per cent. As this is the largest series yet published in Australia, it should be a fair indication of the incidence of syphilis in pregnant women attending hospital antenatal departments. In a comparison of the incidence with that of other countries it is difficult to assess its significance because of the mixture of populations and living conditions.

Of the 160 patients diagnosed as syphilitic, the records are available for 134. Potter and Adair state that spirochetes have not been demonstrated in the placenta or in the fetus before the fifth month of gestation; they state also that infection probably does not occur until about this time, that it is not a common cause of early abortion but that it contributes to fetal mortality in the last half of pregnancy.

The following tabulation shows the previous obstetric history of 98 multiparas.

Group A. No miscarriages or other catastrophes 41 (41.83 per cent)

Group B. One or more miscarriages but no other catastrophes 33 (33.6 per cent)

Group C. Prematurity, neonatal death, or still birth 24 (24.5 per cent)

A tabulation of the previous obstetric history of 98 multiparas tends to support the statement that syphilis contributes to fetal mortality in the last half of pregnancy.

Group A. Forty-one or 41.83 per cent, of the patients had no history of miscarriage nor of premature labor, neonatal death, or stillbirth.

Group B. Thirty-three, or 33.6 per cent of the patients had had a previous miscarriage but no other abnormality. In this group it must be realized that the pregnancies ranged from second to the fourteenth.

Group C. In this group the author found that 24, or 24.5 per cent, of the patients had a history of stillbirth, a neonatal death, or a premature birth. A further analysis of group C showed that some patients had experienced more than 1 catastrophe. This was illustrated by the patient who had had 7 pregnancies: 3 premature labors, 2 miscarriages and 2 stillbirths.

The results of the present pregnancies, based on the records of 134 patients are as follows:

One hundred and twenty children were born alive 8 were stillborn and 4 died in the neonatal period there were 2 miscarriages. The combined stillbirths, neonatal deaths and miscarriages numbered 14 or 10.4 per cent.

This figure of a combined stillbirth and neonatal death rate of 10 per cent is in contrast to the previous combined stillbirth and neonatal death rate of 24 per cent. All of the 134 patients, whose latest pregnancies were analyzed, received treatment, the adequacy of which depended upon how early in pregnancy they had reported to the out patient department of the hospital.

The author makes the plea that the Wassermann test be made a part of routine antenatal examination of all patients. CHARLES BARON, M.D.

LABOR AND ITS COMPLICATIONS

MacLennan H. R.: Contracted Pelvis in Child Birth: A Study of Its Morbid Effects on Mother and Child. *J. Obst. Gyn. Brit. Empire* 1944, 51: 293

It was found that contracted pelvis existed chiefly in the industrial centers in Scotland where the standard of living was low. The incidence of contracted pelvis varied with the incidence of rickets. Where rickets existed contracted pelvis also abounded. Where rickets was not present contracted pelvis was virtually absent.

The author reviewed a series of cases from the Glasgow Royal Maternity Hospital which deals with a larger number of contracted pelvises than any other center in Britain. This series of 1 049 cases were admitted to the hospital over a period of two years. They comprised 15 per cent of the total admissions. The series was made up of 560 primigravidae and 489 multiparae. They were divided into 3 groups according to their pelvic measurements: a severely contracted group in which the true conjugate was $3\frac{1}{4}$ inches or less, a moderately contracted group in which the true conjugate was less than $3\frac{1}{4}$ inches but more than $3\frac{3}{4}$ inches, and a slightly contracted group in which the true conjugate was $3\frac{3}{4}$ inches.

The mode of delivery offers evidence as to the dystocia which was present.

One of the most striking features was the dystocia caused by slight cases of contracted pelvis. Only 41 per cent of all primigravidae with slight contraction were able to deliver themselves spontaneously and among the multiparas, only 36 per cent were successful in this respect. The others required operative interference and that interference was of a major type in an unexpectedly large percentage.

Throughout the entire investigation it was noticed repeatedly that the cases of slightly contracted pelvis play a very large part in producing the morbid effects associated with contracted pelvis. This is a

point of considerable significance, in the first place because the slight cases will tend to increase relatively in number as rickets diminishes in severity throughout the country and, in the second place, because the slight cases may escape diagnosis.

It was observed in the incidence of cesarean section (309 cases in all) that the rate rose sharply from 21 per cent in primigravidas to 39 per cent in multiparas.

Thirty-one craniotomies and 53 high-forceps operations were necessary. Many of the patients were admitted to the hospital after an unsuccessful attempt at delivery with the forceps outside. The risks associated with failed forceps are already widely appreciated and the number of such cases occurring in the present series was 36.

The part played by the child in causing dystocia is an important factor. Unless a child is under average weight and not more than 6.5 pounds there is a poor prospect of spontaneous delivery. In studying the averages of weights and the lengths of labor it appeared that there was only a small margin of safety and that a difference in weight of 0.6 of a pound might affect the prognosis adversely. It was also noted with interest that in cases of contracted pelvis of slight degree severe dystocia occurs with a normal 7½-pound baby. However a number of women deliver themselves spontaneously of babies of 7½ pounds and occasionally of over this weight. The main reason for these spontaneous deliveries is that the patient has stronger uterine contractions, a greater endurance than normal, and is temperamentally suited to bear such pain. She may be said to have a satisfactory "labor equation." If this were not the case and if all patients had a similar labor equation, it would be found that the larger the baby the longer the labor. The statistics show no such correlation. One woman may take longer to deliver a 6-pound child than another to deliver an 8-pound child. It may be assumed that an average woman with an average labor cannot deliver an average child if she has a contracted pelvis—be it slight, moderate or severe. For a spontaneous vaginal delivery the child must be below average weight, the mother must have stronger uterine contractions than the average and she must be temperamentally capable of enduring them.

Stillbirth is more than four times more frequent in cases of contracted pelvis than in cases with normal pelvis.

Protracted labor and instrumental delivery were followed often by puerperal sepsis. Twenty-five per cent of all the primigravidas and 18 per cent of all the multiparas were found to have puerperal morbidity.

The maternal mortality rate for the series was 21 per 1,000 (22 in 1,049). In the normal group it was 3 per 1,000. For the purposes of analyses the cases have been divided into 3 groups. The groups may be defined as follows:

GROUP I The patient died immediately after dystocia associated with trauma, shock or hemorrhage.

GROUP II The patient died after dystocia associated with trauma, shock, or hemorrhage followed later by sepsis or postoperative pneumonia.

GROUP III The patient died after dystocia associated with trauma, shock, or hemorrhage, but a concomitant factor such as high blood pressure or pyelonephritis, rendered the patient more vulnerable.

GROUP IV The patient died after dystocia without undue trauma, shock, or hemorrhage, but delivery was followed by postoperative pneumonia, postoperative peritonitis or other postoperative complication.

GROUP V The patient died when measures had been taken to prevent dystocia for example early cesarean section but were followed by shock, peritonitis or other postoperative complications.

GROUP VI The patient died from a condition unassociated with contracted pelvis, but dystocia was a contributory factor.

GROUP VII The patient died from a condition unassociated with contracted pelvis, but contracted pelvis contributed in some way to the fatal issue.

GROUP VIII The patient died from a condition unassociated with contracted pelvis and the contracted pelvis did not in any way affect the fatal issue.

It will be seen that in the first 4 groups death followed dystocia. 67 per cent of the deaths fall into these groups.

In the 5th group death occurred following measures taken to prevent dystocia. 23 per cent of the deaths occur in this group.

In the 6th, 7th and 8th groups contracted pelvis is either a contributory or only an incidental factor. These latter groups account for only 10 per cent.

It is important to consider what steps may be taken to improve the present position. The first and ultimate remedy must clearly be the prevention of rickets even in the mildest forms, for the investigation has shown that the slight cases of pelvic contraction give rise to as great difficulty today as do the severe ones. It is already well recognized that dietetic and social factors are primarily responsible for the production of rickets. The fact however that methods of preventing rickets are already well known and that rickets in its grosser forms is something so rarely to-day leads sometimes to an attitude of mind which supposes that the danger of rickets has ceased to exist whereas in fact, the condition is still prevalent in minor degrees. By being minor and "masked" it is all the more dangerous to female children when they reach the childbearing age and are discovered to be suffering from contracted pelvis. It will be readily admitted that the first line of defense against rickets is the care of the child by a healthy and intelligent mother. The value of the antenatal clinic cannot be overestimated from the viewpoint of the mother's general health. The nourishment of the mother during pregnancy and particularly during lactation may be of primary importance in producing or preventing rickets in the offspring.

There are two main defects in the system. The first is nonattendance. The second defect is failure on the part of the mother to utilize adequately the advice given at the clinic or by her doctor. This may be through lack of education or facilities.

The investigation has attempted to show the advantage that would be gained if every case of contracted pelvis were recognized before labor so that provision for skilled treatment could be made in ample time. The earlier recognition of contracted pelvis implies an improvement in the general level of antenatal pelvimetry.

In the hospital the greatest care is required for accurate estimation of the degree of deformity present. Today this can be done most satisfactorily by means of roentgenological pelvimetry. It is, of course essential that one of the well proved methods should be chosen.

In a trial of labor when the size of the pelvis has already been ascertained it is essential for the obstetrician to acquaint himself with the quality, duration and frequency of the uterine contractions. Not only is the quality of uterine contractions of importance but the patient's capacity to endure strong contractions must also be borne in mind.

The purpose of this work was to draw attention to the rachitic pelvis which causes such disaster to the mother and her child. The remedies are in our hands. We must apply them.

CHARLES BARON M.D.

Tollefson, D. G. Methergine (Synthetic Lysergic-Acid Derivative) A New Oxytocic. Preliminary Report. *West J Surg* 1944 52 383

Methergine is d-lysergic acid d-1-hydroxybutylamide a synthetic ergonovine derivative. The availability of methergine may come to represent an outstanding achievement in ergot chemistry and therapy because of the scarcity of adequate quantities of rich crude ergot of rye high in alkaloidal content.

Hemorrhage next to infection is the most common cause of maternal mortality. The hemorrhage occurring in the third stage of labor is due to failure of the uterus to contract, therefore any medication which insures a rapid and prolonged effect is a valuable adjunct to our therapeutic armament.

Since the use of analgesia is almost routine in modern obstetrics and the relaxing effect of these pain relieving drugs cannot be denied, it seemed that the use of medication in a group of pregnant patients would be the best possible test.

To 200 patients who received as a minimum 6 gr. of nembutal and 1/100 gr. of scopolamine (many had additional medication and almost all had cyclopropane for delivery) 1 cc. of methergine containing 0.2 mgm. of lysergic acid d-1-hydroxybutylamide was given intravenously as soon as separation of the placenta was in progress. The usual signs of separation are not always reliable but in this series the placenta was palpable in the cervical opening. The action of the oxytocic was rapid and was apparent

on an average in forty-eight seconds. As soon as this contraction was palpated simple expression was practiced and the placenta was expelled almost immediately. Blood loss in this series averaged 98 cc.

During the puerperium, methergine was given in doses of 3 tablets daily for several days and involution of the uterus proceeded satisfactorily. In this series the lochia was noticeably reduced.

The last 200 patients delivered remained in the hospital on an average of eight and four tenths days. Nine patients have been readmitted to the hospital because of excessive flow. Two patients had been given methergine, and both were curetted—one on the twenty-second day, the other on the seventeenth day. Normal endometrium was removed in one, in the other a small placenta fragment was removed.

In 12 patients not included in this series this drug was given before the separation was completed and a powerful contraction of the cervix caused an incarceration of the after birth. In 2 two hours elapsed before the contraction relaxed although bleeding was not excessive.

The author's experience would suggest that the administration of methergine should be delayed until separation is complete or at least in progress.

DANIEL G. MORTON M.D.

NEWBORN

Erickson, C. A.: Rubella Early in Pregnancy Causing Congenital Malformations of the Eyes and Heart. *J. Pediat.*, St. Louis, 1944, 25 381

Three series of cases were reported from Australia in which virus infections, particularly rubella occurring in early pregnancy seemed to be related to congenital defects. The author reviews these and reports an additional 11 cases.

The duration of pregnancy at the onset of the rubella varied from two to ten weeks. Cataracts, microphthalmia or corneal opacity was present in all 11 babies.

Most of the babies were small and experienced feeding difficulties. Congenital heart defects were present in 9 of them. Two were considered mentally retarded and 1 had a severe anemia resembling erythroblastosis.

Important developmental changes occur in early pregnancy, which coincided with the occurrence of rubella. Increased observation may incriminate other virus infections as the cause of congenital anomalies.

The author states that in view of the constant occurrence of serious congenital anomalies in association with rubella in early pregnancy we should seriously consider (1) deliberate exposure at an opportune time in childhood (2) the use of convalescent serum on susceptible pregnant women particularly if they have been exposed (3) therapeutic abortion if rubella occurs during the first two months of pregnancy and (4) research on animals with other types of virus infection.

JAMES F. DONNELLY M.D.

Evans, M. W.: Congenital Dental Defects in Infants Subsequent to Maternal Rubella during Pregnancy. *Med. J. Australia*, 1944, 35

Maternal rubella occurring in early pregnancy is associated with a high frequency of congenital anomalies among which dental defects have been noted. Dental examinations were conducted on infants born of mothers having had rubella in early pregnancy.

Of the 34 babies examined 23 showed congenital dental anomalies major in nature in 18 cases. All but 2 had other congenital defects. The most severe defects were present when the maternal infection occurred between the sixth and ninth week of pregnancy which is considered to be the critical period of dental development. The main abnormalities noted were retardation of eruption, enamel hypoplasia and dental caries.

JAMES F. DONNELLY, M.D.

Swan, C.: A Study of 2 Infants Dying From Congenital Defects Following Maternal Rubella in the Early Stages of Pregnancy. *J. Path. Bact. Lond.* 1944, 56: 189.

Gregg first recorded the fact that mothers who contracted rubella in early pregnancy gave birth to infants suffering from congenital cataract often associated with congenital heart disease.

This report presents the observations made during autopsy on 3 of these infants.

All were small, thin and undernourished. The anterior fontanelle was larger than normal in 2.

Ocular abnormalities were noted in 3 infants. Unilateral microphthalmia was present in one infant, the other eye being cataractous; the other infant had bilateral cataracts. Microscopically the nuclear portion of the lens showed massive necrosis. There was disintegration of the cortical lens fibers which had been replaced by vacuoles. The fibers still living showed swelling, irregular staining and granularity and vacuolation of the cytoplasm. The lens fibers were swollen and pale. Very little reparative effect was seen.

A variable enlargement of the heart was found. The ductus arteriosus was widely patent in all 3 cases, as was the foramen ovale. In 1 there was in addition a defect of the interventricular septum. Microscopically the ductus arteriosus was noted to have a larger lumen and thinner wall than in the controls. The internal elastic lamina was either ill defined or absent.

Atelectasis and bronchopneumonia were present in the lungs of all 3 cases. Minute foci of degeneration and necrosis were found in 1.

In the kidney occasional glomeruli were small and showed partial or complete replacement of their capillaries by hyalinized fibrous tissue. Some proliferation of the parietal layer of Bowman's capsule was seen but it differed from the crescentic type of glomerulonephritis.

No lesions were noted in other viscera.

Considerable evidence seems to indicate the virus of rubella as the cause of these congenital abnormalities.

The mechanism is not clear but it appears that the virus affects the blood vessels primarily.

JAMES F. DONNELLY, M.D.

MISCELLANEOUS

Grossmann, L. L.: The Diagnostic and Therapeutic Use of Prostaglandin: Its Effect upon Pregnancy or Delayed Menstruation. *Wad. J.* 5: 1944 5: 443.

The rationale and use of prostaglandin in diagnosing pregnancy and/or treating delayed menstruation are described.

The drug was employed in diagnosing accurately or in treating effectively 100 cases of delayed menstruation due to pregnancy or some other cause. Patients were injected with 1 cc. of prostaglandin methylsulfate (1:1,000) on three successive days unless bleeding ensued after the first or second injection. In 46 instances when bleeding did not result, pregnancy was correctly assumed to be present. In 4 of these 46 cases the Aschheim-Zondek test was negative at the time of the injections; these patients were later proved to be pregnant. In no case did bleeding occur in the presence of pregnancy so far as could be determined clinically.

The test is inexpensive, simple to apply and does not require laboratory assistance for verification. Apparently uterine bleeding will almost invariably result in cases of amenorrhea not due to pregnancy or endocrine deficiencies, the menopause (3 cases) or gross pelvic disease. The onset of bleeding is due presumably to the production of uterine hyperemia by the drug.

DAVID G. MORROW, M.D.

Pracott, F., and Bazzan, M.: Inhibition of Lactation by Hexoestrol Dipropionate. *Brit. M. J.* 1944 438.

The authors briefly discuss the physiology of lactation and describe the rationale for using estrogen for the inhibition of lactation. Estrogens probably depress the activity of the anterior lobe of the pituitary gland. The absence of suckling plus estrogen administration produces the most satisfactory inhibition of lactation.

A review of the various methods currently used for inhibiting lactation, and their results, includes such substances as stilbestrol, hexoestrol, dienoestrol, trichlorethylene, testosterone propionate, and methyl testosterone. These substances are usually given by mouth over periods varying from three to ten days.

The authors point out that castration of the estrogens retards their rate of absorption and diminution and thus prolongs their action in the body. Hexoestrol dipropionate was found to be not as effective by mouth, but the duration of action was much as long. It was therefore decided to try its effect in the suppression of lactation.

Two groups of patients were used: 23 were given hexoestrol dipropionate by mouth and 44 were given this substance in oil intramuscularly. All patients treated were those in whom it was necessary to inhibit

bit lactation because of stillbirth abortion neonatal death or cracked nipples. The oral dose of hex estrol dipropionate used was between 10 and 20 mgm three times daily for three days. The dose by injection was 12.5 mgm. in one injection within the first three days after delivery.

The results of these treatments revealed that a single intramuscular injection of 12.5 mgm of hex estrol dipropionate inhibited lactation in 66 per cent of the 44 mothers within the first three days of delivery. Lactation did not occur and there were no signs of breast engorgement or discomfort. In the remaining 34 per cent repeated injections brought relief to all but 2 per cent. 18 per cent required treatment for more than three days after delivery.

A further course of injections was necessary to suppress "secondary filling" in only 7 per cent of the cases. This compares well with percentages ranging from 25 to 45 for stilbestrol as reported in the reviewed literature.

Hexoestrol dipropionate given by mouth was not so satisfactory as when given by injection.

HARRY FIELDS, M.D.

Argenti P: Childbirth in the Greek Island of Chios in the Sixth Century B.C. *J Obst. Gyn. Brit. Empire* 1944, 51: 344.

Two Greek terracottas small votive offerings are in the Museum at Nicosia in Cyprus. The one represents a woman being delivered of child in an upright seated position, she is held from the back by another woman, who has her hands clasped round her belly and who is probably pressing the infant downwards exactly as described in "The Expert Midwife" of 1637 and in Sonnini's description written in 1780 in front, and facing her in a kneeling posture, is the midwife with her arms outstretched to receive the after birth. The second terracotta is more coarsely modeled and may be older; it represents a similar scene except that the seat on which the pregnant woman is reclining is missing and from the angle of the thigh it would appear to have been higher; also there is no trace of a third woman supporting from the back the woman in labor.

These terracottas establish the fact that in classical times women were delivered in an upright perpendicular position; also that then in all probability some kind of special labor-stool was in use.

From what Sonnini writes, we may definitely deduce that at the close of the eighteenth century the labor-chair was no longer in use in France. The labor-chair which was in use in Chios until about 1914 was higher than the tripod represented by Sonnini, and had a back in accordance with the ideas expressed in "The Expert Midwife" but instead of being concave to fit the curvature of the body it is straight like an ordinary chair.

In Chios doctors took over, so to speak, from midwives as late as about 1914. The following information was given by an old woman who had practiced midwifery on the island for many years before her retirement.

As there were no means of communication in Chios except a few inferior roads the midwife went on her round on muleback, generally accompanied by an assistant, who for choice would be her daughter and successor-elect to her practice on one side of the mule was strapped the labor-chair which folded up having heavy hinges behind the seat and at the junctures of the arms and back. For padding shaped cushions were tied to the different parts of the chair. The pregnant woman was seated in the chair and in order to bring on the child, was jolted up and down from the back by the assistant who held her under the arms. If the woman was heavy the jolting was carried out by one of the women members of the family who helped by holding the woman under the left arm with her right hand and the midwife's assistant doing likewise on the right side with her left hand thus leaving the right arm of the more experienced assistant free for pressing down the belly of the expectant mother. The midwife's position was exactly similar to that of the one represented in the terracottas dating from 600 B.C. The midwife's after treatment continued for eight days after which the mother was considered to be in condition to resume her normal life.

CHARLES BARON, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY AND URETER

Zide, H. A. Renal Complications of Sulfonamide Administration: Report of Reactions from Sulfathiazole and Sulfadiazine. *J Urol* Balt., 944, 58 75

The case histories of 10 patients with 11 renal reactions to sulfonamides 1 to sulfathiazole and 10 to sulfadiazine are analyzed.

The minimum dosage before renal symptoms occurred was 7 gm. of sodium sulfadiazine given intravenously.

The minimum time before onset of the renal symptoms was twenty four hours.

Two delayed reactions occurred one six days and the other twelve days after sulfadiazine was discontinued.

The urinary reaction to litmus paper during the renal complications was acid in 8 instances and undetermined in 2, and alkaline in 1 instance.

The blood sulfadiazine level ranged from 23 mgm per cent to 4 mgm. per cent at or about the time of reaction being over 8 mgm. per cent in most cases.

The treatment of this series of cases consisted of conservative means in all, with an unsuccessful attempt at manipulative treatment in 1 case which later responded to conservative treatment.

The end-results were cures of the original conditions and renal complications in all cases.

The prophylaxis and treatment of renal complications of sulfonamide administration are discussed.
JOHN A. LOFF, M.D.

Baratz, L. H.: Renal Hydrocele; Subcapsular Renal Extravasation. *J Urol* Balt., 944, 5 84.

In a renal hydrocele the true capsule of the kidney is separated by urine so that the kidney is situated at the base of the sac. The etiology is dependent upon renal trauma and the following associated factors: (1) trauma or perforation which opens the pelvis or calyx, (2) a maintenance of the opening beyond the healing period, (3) an acquired or pre-existing hydronephrosis, and (4) slow extravasation beneath a normal uninjured capsule.

Gross pathology shows the capsule of the renal hydrocele to be composed of Gerota's fascia, perinephric fat and fascia, and renal capsule all compressed and thickened into a shining membrane. On microscopic examination the inner surface shows a single layer of flat, or cuboidal cells on a loose, fibrous connective tissue. The deeper portions of the membrane show elastic fibers and lobules of adipose tissue separated by connective-tissue septa containing engorged capillaries. The sac is of variable proportion and the kidney surface is often characterized by multiple cortical abscesses with areas of coagulation necrosis and involvement of the tubules with eventual autonephrectomy.

The author reports 8 cases from the American literature, all of which demonstrated a urinary extravasation beneath the true renal capsule. It is mentioned that other cases reviewed both from the American and foreign literature did not demonstrate that the sac lining was composed of true renal capsule.

The patient initially presents abdominal discomfort associated with an ever increasing abdominal tumor. The subjective findings of nausea, vomiting and pain appear later along with findings of tachycardia and a low grade temperature, in addition to an elevated total white blood-cell count, secondary anemia, drowsiness and marked weakness. The urine findings are limited to possibly a few white cells and seldom hematuria.

Cystoscopic examination may reveal no drainage of urine from the affected side, and pyelography may be vague because of the mass in the area, which in turn causes ureteral displacement or compression, or both. Furthermore barium in the stomach discloses a roentgen outline of that organ which is forced laterally and anteriorly. The diagnosis of renal hydrocele is established at operation, but with a history of trauma and the discovery of a displaced and compressed ureter the diagnosis of renal hydrocele should be suggested.

The case of a patient thirty-seven years of age, who was found to have a left renal hydrocele after child delivery is reported. The sac was drained and nephrectomy avoided. This patient was treated by aspiration of the urine and the maintenance of free drainage through the operative incision. On the forty-fourth postoperative day no further evidence of urinary drainage was evident from the low wound the patient was discharged from the hospital on her forty-sixth postoperative day. An intravenous pyelogram a month later revealed normal calyceal and pelvic morphology. The case is well illustrated by pyelographic reproductions, and stomach displacement is clearly demonstrated in another reproduction.

In the treatment of renal hydrocele, early operation is imperative. In the absence of extreme toxemia a repair of the calyceal fistula may be feasible. However in extreme toxemia, drainage of the cyst should be performed followed by nephrectomy at a later date. If the suppurative process subsides, subsequent nephrectomy may be avoided, as it is in the case reported by the author.

ROBERT LACK, JR. M.D.

Semana, J. H. Nephrectomy for Hypertension in a Two-and-One-Half Year-Old Child with Apparent Cure for Three Years. *Bull. Johns Hopkins Hosp* 1944, 75 84.

Some difficulty remains in selecting those patients with hypertension who can be permanently relieved

by nephrectomy. The solution of this problem will be aided by reports of cases carefully studied before and after operation. In the case described the blood pressure changed from a maximum preoperative level of 200/134 to one of 98/62 at the time of the last visit, three years after operation. The microscopic diagnosis of the lesion in the extirpated kidney was chronic pyelonephritis. However marked perirenal fibrosis a cause of experimentally produced hypertension in dogs seemed the most important etiological factor in this case. A retroperitoneal teratoma had been removed four months previously from the region of the kidney. Symptoms began following this operation.

The decision to explore the left kidney was based on several considerations. On three occasions intravenous injections of diodrast outlined only the right upper urinary tract. Failure to demonstrate secretion of radiopaque material with x rays in any one instance is not pathognomonic of renal disease but when one of two kidneys is persistently unable to secrete the material in sufficient concentration to cast a shadow, it signifies little or no function on the blank side. Also in this case the left kidney secreted less phenolsulfonphthalein than the right.

At operation there was a large amount of dense scar tissue around the kidney. No constriction of either the renal artery or its extrarenal branches was evident. However in view of the poor prognosis and of the findings suggesting renal disease on the left side nephrectomy was carried out. The elimination of hypertension in this patient for a period of three years shows the relationship between the hypertension and the lesion in the left kidney.

While there was intimal thickening of some of the intrarenal arterioles it seems probable that the perirenal fibrosis may have been a factor in producing this patient's hypertension and that previous removal of the teratoma from the retroperitoneal space resulted in the development of this fibrosis.

JOHN A. LOFF, M.D.

Scott, W. W.: Supernumerary Ureter with Extravascular Orifice. *J. Urol.* Balt. 1944 53: 126

Four cases of supernumerary ureter with extravascular orifice are reported. All occurred in females. These cases bring the total recorded in the literature to more than 300 and according to Thom the actual incidence in the female is twice that in the male although the apparent incidence is much less since the condition is asymptomatic because the ureter empties into the prostatic urethra, seminal vesicle vas deferens or ejaculatory duct.

The embryological explanation for aberrant ureteral insertion in the male is not disputed but in the female, when the ureteral orifice is vaginal, there is disagreement since the vagina is of müllerian-duct derivation. However Winterton's work is mentioned this assumes an initial ureteral insertion with vaginal ectopia in the event of a break through the wall separating the wolffian and müllerian systems. Furthermore, it is reiterated that the most

cephalad pelvis is always drained by the ureter having the more caudad insertion.

Regular normal micturition despite incontinence in the female characterizes the condition. The incontinence though both diurnal and nocturnal, may be either or it may be intermittent. Mulholland collected 9 cases without incontinence.

The history of normal regular micturition and continuous incontinence permits a presumptive diagnosis of extravascular ureter. The diagnosis is confirmed by intravenous and retrograde pyelography.

The finding of a large kidney with the upper portion showing no collecting system strongly suggests duplication. Therefore, these findings and a single ureteral opening on the side, together with the characteristic history of incontinence in a female supply sufficient evidence to warrant surgical exploration of the abnormal kidney.

The authors advise heminephrectomy with partial ureterectomy in the treatment of supernumerary ureter and extravascular orifice. The following résumé of the 4 cases is presented.

Case 1: A girl was first seen at the age of five years for a then diagnosed chronic pyelitis and two years later by retrograde pyelography was found to have a supernumerary ureter with an extravascular orifice. A heminephrectomy and partial ureterectomy were done and the patient has enjoyed good health during the nine years postoperatively.

Case 2: A twenty-one-year-old female was subjected to a right heminephrectomy following the diagnosis of supernumerary ureter with an extravascular orifice which was located in the region of Skene's duct on the right. The postoperative course has been uneventful.

Case 3: A twenty-three-year-old female with urine seepage from birth demonstrated by means of intravenous pyelography a collecting system in the superior segment of the large left kidney shadow and on this finding the diagnosis of supernumerary ureter with an extravascular orifice was made. The left heminephrectomy showed little dilatation of the supernumerary segment which explained the adequate dye concentration in the intravenous urograms.

Case 4: A girl of fourteen years showed no evident extravascular ureteral orifice but pyelography showed on the left side a large renal shadow with no collecting system for its upper portion. On this finding a left renal exploration was done and a double kidney and ureter were found. The upper ureter and pelvis were dilated. A heminephrectomy was done.

ROBERT LUCH, JR., M.D.

Goldstein, A. E. and Berman, E. F.: Ureterocutaneous Transplantation. A New Procedure. *J. Urol.* Balt. 1944 53: 324.

Although ureterointestinal anastomosis is a very satisfactory method of diversion of the urinary stream, ureterocutaneous transplantation is indicated in a considerable proportion of the cases requiring diversion of the urine. The conventional



Fig. 1. Gibson incision.

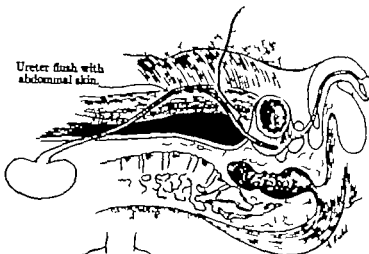
Fig. 3. Loop of ureter exposed.
Internal oblique muscle buried.Fig. 2. Ureter in new position
but still attached to bladder

Fig. 4. Anatomical relationship.

operation of ureterocutaneous transplantation has had several disadvantages: namely, perireteral infection with abscess and slough of the ureter; retraction of the ureteral stump; stricture or kinking of the ureter; and insufficient length of the ureteral stump to permit of a properly adjusted apparatus.

A new technique of ureterocutaneous transplantation, the fundamental principle of which is the establishment of the "right of domicile" of the ureter on the anterior abdominal wall, is described. At the first stage of the operation the ureter is approached through a Gibson incision extraperitoneally and is bluntly dissected free down to the bladder. A loop of silk is passed around the ureter and the ends are led out to the skin to assist in locating the ureter at its junction with the bladder at the second stage. The internal and external oblique muscles and fascia are united behind the ureter, which makes it a subcutaneous structure. No sutures are placed in the ureter and the ureter is not opened at the first operation. It is desirable but not always possible to introduce an indwelling ureteral catheter through the cystoscope preoperatively in order to provide drainage and prevent kinking of the ureter during the three to seven days between the two stages. During this interval the ureter is stretched somewhat and new sources of blood supply are obtained. Leaving the apex of the ureter in the subcutaneous tissues

also provides for observation of its blood supply at frequent intervals.

At the second stage the distal end of the ureter is ligated and phenolized and the proximal portion is brought out as a 3 to 5 cm. ureteral stump. A urethral or Foley catheter is inserted into the pelvis of the kidney to provide drainage. Cystectomy may be performed at the second stage of the operation. The authors consider the use of a cupping device theoretically more suitable than an indwelling catheter but they have been temporarily unable to obtain satisfactory appliances.

Three cases are reported in which this method has been employed. Two were carcinomas of the bladder (1 following nephrectomy for carcinoma of the renal pelvis), and one was severe encrusted cystitis with congenital absence of one kidney. In all of these cases the urinary output was considerably reduced during the first three days following the first stage of the operation, which indicated that the ureter was partially obstructed. In 1 case the output was only 100 cc. per day for the first three days and in another case there was no output for sixty-four hours and the blood urea was 120 mgm. per cent.

The resultant ureteral stumps in these 3 cases certainly warrant the added time required to prepare them. The retrograde pyelograms show that the course of the ureter is direct and free from angulation.

lions. Thus far the procedure has not been performed bilaterally, but the authors believe that should the indication arise it might be done with equal success.

DONALD F McDONALD, M.D.

BLADDER, URETHRA AND PENIS

Ross, J. C.: Injuries of the Urinary Bladder. *Brit J Surg* 1944, 32: 44.

The communication opens with the statement that a dark shadow still hovers over the subject of injured bladder, and although the condition is not common in civilian emergency surgery it occurs in modern warfare. In civilian life bladder injuries are primarily due to automobile accidents and are almost always associated with fracture of the pelvis.

Bladder injuries are divided into three types: (1) contusions such as occur in long labor; (2) wounds, such as occur in penetrating wounds and vaginal hysterectomy; and (3) rupture such as occurs after a blow to the hypogastrium in inebriates and after overdistention during cystoscopy.

Clinically the injuries are divided into the intraperitoneal and extraperitoneal types; the former usually caused by abdominal trauma and the latter usually the result of pelvic trauma. Intraperitoneal injuries usually affect the dome and posterior wall of the bladder with resulting peritonitis; extraperitoneal injuries are usually located anteriorly, laterally or at the base of the bladder and cause extravasation with resulting pelvic cellulitis. The author confirmed these findings by work upon the cadaver.

The prognosis has been found to be in direct relation to the time interval between rupture and repair. Hamilton Bailey is quoted as having an 11 per cent mortality if operation is performed within twelve hours of injury; 55 per cent if operation is delayed for twenty-four hours; and 100 per cent if no operation is performed.

The diagnosis of ruptured bladder may be made on the basis of the history, degree of shock, inability to void, degree of stranguria, plain x-ray film and intravenous urogram, if facilities are available, and the presence of blood when a urethral catheter is passed. The author believes that cystoscopy is permissible if it is considered justifiable to insert a urethral catheter and inject sterile saline solution. He condemns the use of a 2 per cent sodium iodide for cystograms and of air for pneumocystograms.

The author advocates exploration and repair of all abdominal viscera, excision and suturing of the bladder wound and closure of the peritoneal cavity with or without drainage in cases of intraperitoneal rupture. Suprapubic drainage of the bladder is mandatory. Extraperitoneal injuries should likewise have suprapubic exploration with suprapubic drainage of the bladder. Sulfonamide preparations should be used as indicated.

Four illustrative cases with subsequent complete recovery are presented. The article is supported with an ample bibliography.

CHARLES C. HIGGINS, M.D.

MISCELLANEOUS

McCahey J. F., and Fetter J. S.: Nonfibrous Vesicoureteral Obstruction. *J Urol* Balt., 1944, 52: 216.

The authors' purpose in presenting this article is to demonstrate that vesicoureteral obstruction may exist without an organized stricture. Their view is not shared by current urologic opinion which assumes that if there is no hindrance to the passage of a ureteral catheter upward there is no hindrance to the flow of urine downward.

Five cases are presented in which pyelography demonstrated some degree of dilatation of the renal pelvis or ureter or both. In 4 of the cases the presenting symptom was renal colic; in the fifth case hematuria was the complaint. One case of renal colic following retrograde pyelography showed dilatation of the pelvis and ureters but no stricture of the ureter could be demonstrated. Two days later the intravenous pyelograms were normal. One case was treated by ureteral meatotomy and periodic dilatations with good end results. Another case of unilateral renal colic unassociated with demonstrable stricture of the ureter showed dilatation of the pelvis and ureter on the intravenous pyelogram. Catheterization of the ureters relieved the pain, and two days later the pyelograms were normal. On the intravenous pyelograms of a male with a two-month history of intermittent attacks of pain in the right loin a narrowing of the ureter at its junction with the pelvis was demonstrated. Retrograde pyelograms showed that there was no stricture in this region but periodic dilatations of the ureter resulted in relief of the painful attacks. The case in which hematuria was the presenting complaint showed bilateral hydronephrosis and hydroureter. Ureteral dilatation resulted in cessation of the hematuria.

The authors conclude on the basis of these studies that the fact that ureteral catheterization offers no difficulty is not proof that obstruction does not exist at the vesical end of the ureter. Nonfibrous vesicoureteral obstruction should be considered whenever suspicion of obstruction is justified by urologic findings. Continued dilatations may be necessary in some instances of vesicoureteral obstruction. Proper management may be not only pain-relieving but life-prolonging.

DONALD F McDONALD, M.D.

Whitehill, R. and Miller M. H.: Infestation of the Genitourinary Tract by *Strongyloides Stercoralis*: a Case Report. *Bull. Johns Hopkins Hosp.*, 1944, 75: 169.

Strongyloides stercoralis is a human parasite whose usual habitat is the small intestine. The authors recently encountered a patient in whom larvae of this worm were present in the urine. Because of the extreme rarity of this finding they thought it worth while to report the case.

A twenty-two-year-old, white single sailor was admitted to a South Pacific base hospital on April 17, 1944 because of frequency, nocturia and ur-

gency. As long as he could recall he had diurnal frequency up to 10 times. He had nocturnal enuresis until the age of sixteen. After the enuresis cleared he had nocturia 2 times every night. Also for as long as he knew he had some urgency, most marked early in the morning. For two months the urgency was more severe and there was occasional incontinence in the early morning. Five days before the admission a routine urinalysis performed in the base hospital showed a rhabditiform larva of *strongyloides stercoralis* in the centrifuged sediment. Urinary sediments were examined daily during the period of hospitalization. Over the first ten days rhabditiform larvae of *strongyloides stercoralis* were observed on 4 occasions. Occasional urines also showed a trace of albumin, a few white cells and granular casts. Urine cultures were sterile. Numerous stools were negative for *strongyloides* but contained ova of *trichuris trichiura*. The external genitalia and prostate gland were normal. The prostatic fluid was normal. The urethra was normal. There was a small slightly trabeculated area on the posterior bladder wall and a few small areas of infection in the mucosa. The trigone was slightly infected. The vesical orifice was slightly irregular with a small polyplike projection at 2 o'clock. Both ureters were patent without obstruction to a #6 whistle tip catheter with a small bulb. Retrograde pyelograms were normal.

Treatment of the *strongyloides* infestation consisted of enteric-coated capsules of gentian violet (0.06 gm) given by mouth after each meal from April 28 to May 12, 1944. After a week of this medication the symptoms of nocturia, urgency and incontinence cleared. Diurnal urinary frequency decreased to 6 times. The *strongyloides* also disappeared from the urine which was examined daily.

JOHN A. LOER, M.D.

Thompson, G. J.: The Clinical Use of Penicillin in Genitourinary Infections. *J Am Med Ass* 1944, 126: 403.

Five hundred cases in which a diagnosis was made of gonococcal infection of the urethra or its adnexa and 100 cases in which the patient suffered from various nonspecific infections of the genitourinary tract were treated by various methods of administration and various dosages of penicillin. Apparently effective and most convenient in most cases was the intramuscular injection of 20,000 units every three hours for five doses. In the gonorrheal conditions

failures were reduced to 2 per cent with this method, and even these so-called failures were, in uncomplicated gonorrheal infection, cured by subsequent courses of penicillin injection. In no case did the infecting organism prove to be penicillin-resistant, and in no case was there local reaction or systemic reaction even after large doses (500,000 units), which suggested that even larger doses might be employed. In the 10 complicated gonorrheal conditions (epididymitis, prostatitis, seminal vesiculitis) adequate penicillin medication resulted in dramatic improvement as a rule, even in the 6 patients with gonorrheal arthritis the concurrent gonorrheal infection in the urethra and prostate quickly subsided, although the joint condition was not obviously influenced.

Results in the nonspecific genitourinary infections were satisfactory in 4 patients with acute prostatitis (1 with accompanying keratitis), 6 cases of balanitis, 3 infected wound infections, to 24 of 30 patients with chronic prostatitis, in 33 of 36 with urethritis, in 7 of 8 with acute epididymitis, and in 8 of 10 with pyelonephritis. In the 3 instances of interstitial cystitis there was no improvement ascribable to the penicillin treatment. In general, improvement was not so dramatic or so rapid as in the gonorrheal infections, and medication seemed more effective against the Gram-positive organisms, nevertheless, penicillin combined with other urinary antiseptics might well be superior to other forms of treatment.

JOHN W. BRIDGMAN, M.D.

Nelson, R. A.: Penicillin in the Treatment of Granuloma Inguinale. *Am J Syph* 1944, 28: 611.

Encouraged by reports of Mahoney on the treatment of early syphilis with penicillin, 2 negro males, thirty-three and forty-three years of age, respectively, both apparently with chronic syphilis of long standing and both suffering with chronic granuloma inguinale (by Donovan bodies on biopsy) were treated with large amounts of penicillin. One was given 1,800,000 units intramuscularly in fifteen days, and the other 2,360,000 units in four and a half days.

After cessation of the treatment these patients were under observation for from thirty to forty days, and during this time no significant change was observed in the lesions—bilateral inguinal ulcers, and prepuceal ulcer in both patients. Donovan bodies were still present in the tissues of the first patient at biopsy twenty-seven days after therapy was begun.

JOHN W. BRIDGMAN, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Raizenstein, E. C. Jr. and Albright, F.: Paget's Disease: Its Pathological Physiology and the Importance of This in the Complications Arising from Fracture and Immobilization. *England J. M.*, 1944, 231-343.

Attention is called to the occurrence of acute atrophy of bone (osteoporosis) as a complication of Paget's disease and the seriousness and implications of the situation as illustrated by a detailed case history. Discussed briefly are normal bone metabolism, the metabolic abnormalities in osteoporosis as opposed to those in osteomalacia and osteitis fibrosa generalisata, the morbid anatomy of Paget's disease, and finally, a concept concerning the pathological physiology in Paget's disease.

The fact that bone lesions of Paget's disease are not generalized but spotty in their distribution, is strong evidence against the disturbance being on an endocrinological or metabolic basis. The initial lesion is bone destruction, the cause of which is obscure. The resultant weakness of the involved bones renders them less resistant to stresses and strains and this leads to a stimulation of the osteoblasts and an overproduction of bone. The repair of bone by the osteoblasts is never completed since the localized initial disorder causing bone destruction apparently persists. There results alternating destruction and repair of bone, which eventually leads to the pathognomonic pathological finding the so-called mosaic structure. In osteitis fibrosa generalisata bone is destroyed that can best be spared while in Paget's disease bone is destroyed without regard to structure.

If a bone containing Paget's disease is immobilized, as after a fracture the following events occur: the lack of stress and strain in all probability abetted by the alarm reaction of Selye, curbs the over activity of the osteoblasts and the serum phosphatase level, an index of bone formation, falls. The initial disturbance causing bone destruction persists. There results a marked imbalance between bone destruction and bone formation. The increased calcium and phosphorus coming from the bone leads to hypercalcemia and hyperphosphatemia. The capacity of the kidney to excrete calcium may be overtaxed with a resulting hypercalcemia, and if fluids are not forced the diet is not kept low in calcium and immobilization is not kept at a minimum a so-called "chemical death" from hypercalcemia may supervene. Although, in Paget's disease the broken bone becomes decalcified as a whole the fracture site shows a rapidly forming and calcifying callus. This is best explained by the hypothesis that some local influence which stimulates the osteoblasts is set loose at the site of the fracture.

EMIL C. ROBITZKE, M.D.

FRACTURES AND DISLOCATIONS

Blount, W. P. Schaefer, A. A. and Fox, G. W.: Fractures of the Femur in Children. *South. M. J.* 1944, 37: 481.

An attempt is made to correlate the findings in the literature with those in an eight year end result study of 280 cases of fracture of the femur conducted at the Milwaukee Children's Hospital. Of 281 fractures 50 were in the upper third of the femur 104 in the middle third and 37 in the lower third. Of the 104 fractures of the middle third 93 were transverse 99 oblique and 2 greenstick fractures. Comminuted fractures are much rarer in children than in adults. Transverse fractures are likely to be associated with direct trauma, while the long spiral ones are more frequently the result of indirect trauma. Greenstick fractures are less common in the middle third than in the lower third.

Traction is used routinely in the treatment of fractures of the femur in children up to the ages of four and five the overhead traction of Bryant is recommended. The Russell traction method is their choice of treatment for older children, to be used for an average period of from four to six weeks. The patient should be kept in bed for a week or more after the removal of the traction but physical therapy and the routine use of the Thomas walking caliper or cast application following traction are unnecessary. In occasional cases of skeletal traction a Kirschner wire passed through the tibia is recommended. The need for open reduction exists only in fracture at the epiphysis. Follow-up of the patient for a year or more after the fracture has healed is an important part of the treatment. Shortening and overgrowth are of considerable practical importance. Either one may be well corrected by arrest of growth of the distal femoral epiphysis of the longer femur at an appropriate age. The surgeon's duty is not fulfilled to his patient until the child has been discharged with legs of equal length several years after the date of the fracture or after closure of the epiphyseal lines.

Fractures of the lower third of the femur were found to be ideally treated by the Russell method. Epiphyseal displacements are apt to be associated with serious local circulatory disturbances and should be treated as surgical emergencies.

Fractures of the upper third of the femur are treated essentially the same as those of the middle third, with important exceptions. Failures are frequently due to the way the method is applied rather than to any fault of the method itself.

Fractures through the epiphyseal lines at either end are difficult to treat and fraught with grave danger of complications. In the authors series there were only 3 fractures of the neck and trochanter. In greenstick fractures of the trochanter in small chil-

dren, the Bryant traction or plaster fixation in abduction is adequate. In older children with fractures of the neck of the femur, it is desirable to use the abduction traction cast of Hoke. In children of twelve or more internal fixation is sometimes justified.

EMIL C. ROSENBERG, M.D.

Tyner F. H. and Hilleman W. T.: March Fracture; an Analysis of 166 Cases. *Am. J. Roentg.* 94:4, 5 65

The term march fracture, as it is generally understood, applies to those fractures of the metatarsal bones which occur without great trauma, during a march. Due importance to the theory of small repeated traumas incurred in long marches has been given but all authors agree that some other factor must be involved before march fracture occurs.

The authors studied 166 cases, securing accurate information as to the time that the fracture occurred after the beginning of the march, the foot involved, as well as which metatarsal. The blood chemistry was studied in 12 cases. Case reports are given in detail in 3 cases.

The most important factor in the production of these fractures is the increased stress on the metatarsal bones induced by muscular fatigue.

EMIL C. ROSENBERG, M.D.

Krause, G. R., and Thompson, J. R., Jr.: March Fracture; An Analysis of 200 Cases. *Am. J. Roentg.* 94:4, 53 8

The results of a study of 200 soldiers who sustained 220 march fractures of the metatarsals between May 1941 and August, 1943 are presented. Special attention is given to possible predisposing factors and the various theories which have been advanced to explain the pathogenesis of these fractures are discussed. The clinical findings and roentgenological appearances are described in detail. Forty-four per cent of the fractures were in the second metatarsal, 51 per cent in the third and 5 per cent in the fourth. The great majority of the soldiers in this series of cases were infantry men. The length of service prior to the onset of symptoms varied from one month to seven years and ten months, but 80 per cent of the fractures occurred during the first six months of service. Eighty-one per cent of the patients were between eighteen and twenty-nine years of age. Many volunteered the information that the onset of the pain occurred toward the end of a long march.

The immediate cause of the fracture is the rhythmically repeated subthreshold traumas incident to marching which acting by summation reach a point beyond the ability of the bone to bear stress. Fatigue of the calf muscle causes these subthreshold injuries to be accentuated.

A control group of 400 cases was also studied. One half of the fractures are seen and can be diagnosed before callus formation occurs. The fractures vary in extent from a narrow "hair line" to actual comminution. Seven per cent could not be diagnosed on

the first examination but were apparent on re-examination in a few days. Careful study of technically perfect roentgenograms is a requisite. Conservative treatment restores these men to duty with a minimum of time lost. EMIL C. ROSENBERG, M.D.

ORTHOPEDICS IN GENERAL

Frankel C. J.: The Treatment of Acute and Subacute Anterior Poliomyelitis. *Laryng. & Month.*, 1944, 71 451

The author has used the Kenny method of treatment of anterior poliomyelitis at the University of Virginia Hospital for over a year following Miss Kenny's tenets scrupulously. His conclusions were that the patients were made more comfortable by the applications of hot packs, and that the Kenny system of physical therapy had some merit. He could see no reason, however for the system of rigid, almost ritual-like, rules laid down by Miss Kenny nor were her explanations of various phenomena valid.

He found the Kenny treatment expensive. It required large numbers of trained personnel, few of whom are now available. In view of his indifferent results, he has discarded the full Kenny treatment and has returned to the so-called orthodox method, however he utilizes a few of the routines advocated by Miss Kenny.

The patients are being placed on firm beds, supplemented by fracture and foot boards. This is the type of bed advocated by Sister Kenny and in his opinion provides excellent immobilization.

Muscle checks are made by trained physical therapists as well as by the orthopedic staff, and all painful muscle groups are treated with the hot wet packs.

The method of application as suggested by Sister Kenny carries with it practically no danger of skin burn and therefore is to be recommended over methods more easily applied. However the author does not apply the packs more often than four or five times daily because personnel requirements are sharply with more numerous applications than this. Prostigmine, methyl sulfate and atropine are being administered subcutaneously for one dose and after that prostigmine bromide and atropine are given three times daily. Recent work has shown that these drugs play a definite part in relieving muscle spasm.

When muscle pain subsides physical therapy is instituted. Muscle checks are made about once every month and hot packs are discontinued with the disappearance of pain and limitation of motion.

As soon as is feasible ambulatory braces are applied.

Cases which show no progress within a period of six months are generally considered hopeless so far as future recovery of the affected parts is concerned, and ambulatory braces should be applied. No surgery is contemplated for at least one year or eighteen months after the onset of the disease.

Precautions should be taken against exposure to flies. These insects are known to be able to carry

and distribute the virus particularly when excreta from patients in the acute stage of the disease has not been disposed of properly.

An examination should be made of the extremities by practitioners to determine the sites for the hot packs. Both legs should be lifted carefully from the bed and if the patient complains of pain in the hamstring area that site should be noted for application of the hot packs. The feet should be dorsiflexed to demonstrate pain in the calf group. Sitting the patient up and flexing the neck will demonstrate involvement of the neck muscles. Abduction of the arms will demonstrate pain or involvement in the pectoral or shoulder area, and movement of the elbow and wrist will bring out pain if present in those parts.

The author has found that the rigid bed is more simple and appears to be more satisfactory than splints or casts. There is, however, no valid objection to the use of these splints.

Other methods of heat have been tried they include hot paraffin diathermy infrared electric pads hot water bottles, and heat cradles but none have as yet proved as efficacious as the hot woolen pack when well wrung out.

ROBERT P. MONTGOMERY, M.D.

Chance, B. Jr.: Evaluation of the Kenny Method in the Treatment of Chronic Infantile Paralysis. *Pennsylvania M. J.*, 1944, 47: 975

The author evaluates 23 cases of chronic infantile paralysis treated according to the Kenny method. The patients selected had their disease from one to five years and had previously received the best of orthodox physical therapy. They were all carefully evaluated on the basis of their previous rate of improvement, and the majority had in the author's opinion reached a stage in which little or no further improvement could be expected with the usual type

of physical therapy. All of the cases displayed the following symptoms: (1) muscle spasm, (2) incoordination, and (3) loss of tone, reflexes and the ability of voluntary contraction described under the Kenny concept as "mental alienation."

Two forms of treatment were carried out. The first was the application of hot fomentations for the relief of muscle spasm. These were made of wool blanket material wrung out of boiling water and applied directly to the skin in packs for two-hour periods. The second phase of the treatment was that of muscle education. Individual muscle function was stressed and attempts were made to make the patient aware of the correct action of each muscle. Careful records were kept at all times. Limitation in joint motion was measured and photographed at frequent intervals. Increase in the range of joint motion was taken to be an indication of release of the muscle spasm. In all cases the previous treatment and the rate of improvement were well known and all of them were treated by the same technicians as previously.

After from three to eight months of this treatment the author noted a decrease in muscle spasm in all of the cases. Release of muscle contracture was noted in all but 7 cases. Seventeen of the cases showed marked improvement and all of the cases showed some over all improvement. One factor noted in the improvement was the excellent psychological influence of the treatment. The author stresses that the Kenny treatment must be directed at the clinical manifestations of spasm and carried out only when indicated. Cases must be carefully selected if good results are to be obtained. Complete prolonged paralysis of antagonistic muscle groups associated with the destruction of anterior horn cells in the spinal cord cannot be helped either by the Kenny treatment or any other type of physical therapy now in use.

DAVID H. LEVINTHAL, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Elkin D. C.: *Vascular Injuries of Warfare*. (1st ed.) Surg 1944, 120-184.

Vascular war injuries may be classified in three groups: the first consists of those cases in which the blood vessel is either completely severed or in such a state of vasospasm as to cause death of the tissues it supplies; the second consists of cases in which an already existing vascular lesion is activated by the trauma of military service; and the third consists of cases of arteriovenous fistula or aneurysm.

Arterial occlusion may be either partial or complete. With total occlusion gangrene or ischemic paralysis will result unless an adequate collateral circulation is established. Arterial spasm results from trauma to the vessel wall itself or to the tissues about it. Vasospasm may be segmental or sufficiently reflex in character to produce a total vasomotor imbalance of an extremity. If this condition is not relieved, thrombosis with fibrosis, atrophy and deformity and even gangrene will develop. Reflex vasoconstrictor impulses may be removed by periaxillary sympathectomy, ganglionectomy or procaine sympathetic block.

Pre-existing vascular lesions such as vascular nevi, congenital telangiectasia, or angiomas, may become circoid aneurysms, pulsating angiomas, and arteriovenous aneurysms when activated by trauma. Twelve cases with such histories are reported. These lesions may be treated in a variety of ways, i.e., ligation of the main blood supply, multiple circumferential sutures, or the injection of sclerotic agents.

Early in the inception of arteriovenous fistula, no symptoms or physical signs may be noted other than an auscultatory bruit. Other signs and symptoms may be masked until the edema or the hematoma of trauma subsides. An arteriovenous fistula can be differentiated from a false arterial aneurysm by detection of a continuous thrill and bruit accentuated

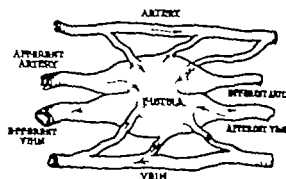


Fig. 2. Schematic drawing to show communications between an artery and a vein, illustrating the necessity of not only quadruplication but complete excision with all branches.

in systole. Other characteristic manifestations of an arteriovenous fistula are dilatation of the vein about and distal to the fistula, and slowing of the pulse with obliteration and trophic changes of the extremity. With large fistulas, cardiac dilatation may be demonstrated with x-rays. Treatment should be deferred to allow for the maximal development of a collateral circulation unless cardiac failure is imminent. To be successful, operation requires that the fistula be completely excised or obliterated. Ligation alone is often followed by recurrence through the collateral circulation. When excision is not possible, the fistula may be infolded by heavy mattress sutures. The operation should be done without the use of a tourniquet.

In the discussion BUCK stated that vasospasm may develop after nonpenetrating wounds, simple fractures of the long bones after severe wounds, and the presence of various types of superficial infections, such as trichophytosis. Vasospasm may be the deciding factor in gangrene of a part and influence the development of gas infection. Sympathectomy should be done more commonly.

The Alatas technique for the treatment of arteriovenous aneurysms was discussed and RIVES demonstrated the value of obliterative aneurysmorrhaphy by a series of case reports and claimed that it offered the best method of preservation of the collateral circulation and required a minimum of dissection.

WATKINS referred to the work of Blakemore and Lord who have devised a nonsuture method of bridging gaps in arteries with vein grafts on vitallium tubes which permits re-establishment of arterial continuity.

BENJAMIN G. P. SHERIDAN, M.D.

Bigger I. A.: The Treatment of Traumatic Aneurysms and Arteriovenous Fistulae. Arch Surg 1944, 49-170.

Twenty-nine cases of traumatic arterial aneurysm or arteriovenous fistula have been studied by the

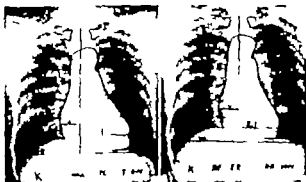


Fig. 1. Showing enlargement of the heart and return to normal size following excision of an arteriovenous aneurysm. (Courtesy of J. B. Lippincott Co.)

authors. Thirteen of the patients had arteriovenous fistulae 15 had arterial aneurysms and 1 had an aneurysm of the abdominal aorta and a fistula between the aorta and the vena cava.

A traumatic arterial aneurysm is usually the result of injury to an artery deeply embedded in the soft tissues. In the early state the lesion is called a pulsating hematoma, but when it becomes well localized and spherical it is called a traumatic or false aneurysm. This article is concerned with the latter condition.

It is generally agreed that once localization has occurred, surgical intervention should be delayed to permit improvement in the collateral circulation and disappearance of bacteria from the adjacent tissues. Unless complications which demand earlier operation arise, conservative treatment should be continued for at least from six to eight weeks.

The interruption of nerve function by the pressure of an expanding aneurysm is not necessarily an indication for excision of the aneurysmal sac, for any procedure which relieves pressure such as aneurysmorrhaphy if performed early will be followed by return of nerve function. It is important therefore, that a careful neurological examination be done on any patient with a traumatic vascular lesion especially when the subclavian axillary brachial, or popliteal artery is involved.

Infection alone may be treated conservatively but careful watch must be kept for secondary hemorrhage and if it occurs immediate operation is indicated. The type of operation is dependent on the extent and severity of the infection as well as on the location of the aneurysm. If the infection is mild and especially if the aneurysm is so located that exposure of the artery proximal to the infection is difficult or fraught with unusual danger the sac may be opened and the artery doubly ligated and completely divided between the ligatures. If on the other hand the artery can be readily exposed proximal to the area of infection and obstructed without interference with essential collateral channels proximal ligation of the artery and of the concomitant vein may be the treatment of choice.

Excision of an aneurysmal sac is more certain to cure the lesion than aneurysmorrhaphy but has the disadvantage of destroying more collateral channels than does the intrasaccular operation. It is reasonable to assume that interference with the collateral arteries would increase the danger of ischemic gangrene and would also increase the degree of chronic circulatory deficiency.

An atypical or incomplete operation may result in cure of a traumatic aneurysm but an arteriovenous fistula is rarely cured except by complete ligation of the involved vessels and excision of the fistulous area or by suture of the artery. If the latter procedure is employed it is usually better to ligate the vein above and below the fistula and then to open the vein and suture the artery under direct vision.

Evidence presented by the author indicates that although the excellent collateral circulation developed

in the presence of an arteriovenous fistula makes the danger of ischemic gangrene almost negligible it does not prevent persistent circulatory difficulty when main vessels are ligated and resected. It is therefore suggested that when such important vessels as the carotid artery and jugular vein, the common femoral vessels or the popliteal vessels are the site of an arteriovenous fistula, transvenous repair of the artery be employed if there are no contraindications. The most important contraindication to arterial suture is calcification of the wall of the artery in the area to be sutured.

When main vessels are obstructed especially those to the lower extremity permanent interruption of the sympathetic nerves to that extremity may help prevent chronic circulatory deficiency distal to the obstruction.

JOSEPH K. NARAT, M.D.

BLOOD TRANSFUSION

Messle, E., Stillerman, H. S., Wright, C., and Minnich V: The Effect of the Administration of Digitalis on the Coagulability of Human Blood. *Arch. Int. M.*, 1944, 74: 173

Oral therapeutic doses of digitalis caused the clotting time determined by the Lee-White method to be accelerated in each of 24 patients during the period of administration of the drug. The prothrombin time, measured, in about half of the cases by the Smith bedside method was not altered nor were changes observed in clot retraction. After the administration of digitalis was discontinued the coagulation time increased in the majority of the 13 patients so studied, even though the drug had not yet been completely excreted during the period of observation. It is suggested that digitaloid drugs may have a thromboplastic effect on the clotting mechanism.

WALTER H. NADLER, M.D.

Crawford, T., and Nessim, J. R.: Unusual Response to Dicumarol Therapy. *Lancet*, Lond. 1944, 247: 404.

The synthetic antithrombotic substance dicumarol is coming increasingly into use in cases of venous thrombosis and in other conditions in which it is desired to diminish the clotting power of the blood. The case reported shows some of the difficulties which may arise during the use of the drug. It also illustrates that dicumarol may take very much longer than the usual forty-eight hours to act and its effect may last days after dosage ceases.

A soldier, aged nineteen years, was admitted to the ophthalmic department of a military hospital complaining of flashes of light before his eyes and increasing blurring of vision during the last three months. There was nothing relevant in his previous health or family history.

He was a young man of excellent physique and in good general condition. His blood pressure reading was 130/80 mm. Hg. Nothing abnormal was detected on physical examination with the exception of the eye findings. Vision in the right eye

was reduced to perception of hand movements only at 3 ft., while that in the left eye was 6/60. Bilateral thrombosis of the retinal veins was found.

In view of the fact that the thrombotic process was extending and vision deteriorating, it was decided to administer a course of dicumarol with the object of diminishing the clotting power of the blood and in the hope of checking the progress of the disease. Treatment was begun on September 30, 1943 with a dose of 300 mgm. of dicumarol and thereafter 200 mgm. were given each day after the prothrombin time had been determined. The prothrombin time increased disappointingly slowly, reaching only thirty seconds after thirteen days of treatment. Because of this slow response the dose of dicumarol was increased to 225 mgm. on the fourteenth day and to 300 mgm. on each of the three succeeding days. The drug was then discontinued because of the development of signs of intolerance. On the tenth day of treatment the patient complained of headache, nausea and constipation. On the thirteenth day there was complaint of backache. On the seventeenth and last day of the dicumarol treatment he developed pain in the abdomen and back, and vomited several times.

When the dicumarol administration was stopped the prothrombin time had reached thirty-six seconds. Two days later it rose to thirty-nine seconds and gross hematuria began. Later this day a subconjunctival hemorrhage appeared in the right eye and a transfusion of a pint of fresh blood was then given. This reduced the prothrombin time to twenty-nine seconds but free hematuria continued. On the fourth day after cessation of the treatment the prothrombin time reached a peak figure of forty-seven seconds. Subconjunctival hemorrhage had now appeared in the left eye and had extended in the right. Hematuria was more profuse. A transfusion of 2 pints of fresh blood was given and the prothrombin time fell to twenty-five seconds. Two days later however it had again increased to thirty-five seconds and a third and final transfusion of 2 pints of fresh blood was given. Thereafter the prothrombin time fell to its original value of twenty-two seconds and remained at this level with only minor fluctuations. Gross hematuria continued for a further five days (eleven days in all) after which there was microscopic hematuria for six days before the urine became normal. All symptoms associated with the dicumarol gradually subsided. Six days after cessation of treatment the blood pressure had fallen from 160/90. The drug appeared to be without effect on the retinal venous thrombosis.

The points of interest arising from this case are the delay in the development of the antithrombotic action of dicumarol in a patient who later reacted strongly to the drug; the signs of gastric and renal irritation which preceded the hemorrhage and the long period of action of the drug after its administration had been stopped.

It is evident that at present great caution must be exercised in increasing the dose of dicumarol when

the response to ordinary dosage is unusually prolonged. In addition it is clear that in using this drug the physician or surgeon must be prepared to administer repeated transfusions of fresh blood should hemorrhage occur and a close watch must be kept on the prothrombin time for at least a week after administration of the drug has ceased. The action of dicumarol is in contrast to the more physiological action of heparin.

JOHN E. KIRKPATRICK, M.D.

Scott R. A. M., and Lissimore, N.: *Mesenteric Thromboses in Lymphatic Leucemia Treated with Dicumarol*. *Lancet* Lond. 1944, 247-49.

The authors report the case of an active man aged sixty-two years who had been healthy until at the age of forty-five he noticed shortness of breath on climbing, and increasing fatigue at the end of the day. Occasionally he had taken iron for anemia.

Episodes of cramping pain in the abdomen, of short duration began in July 1941. On one occasion a few months later he was seized with abdominal pain and vomited "coffee grounds." He recovered promptly. On February 12, 1942, he had violent abdominal pain and the familiar vomiting and diarrhea which became more severe. He went into shock which subsided with the administration of frequent doses of morphine and atropine. Another attack occurred on February 26, 1942.

A surgeon diagnosed an acute abdomen and a laparotomy was performed. A thrombus in a branch of the superior mesenteric vein was found; it was causing an acute intestinal obstruction of the terminal ileum. The spleen was enlarged. Due to the emergency a complete blood count was not performed until after surgery. (The total leucocyte count was 180,000, 95 per cent of these cells being lymphocytes.)

Attack followed attack until a two-weeks course of x-ray therapy was given to the spleen and enlarged glands of the neck, beginning on August 15, 1942. This improved the blood picture and reduced the total leucocyte count to 11,200 (50 per cent lymphocytes) by August 26, 1942. Between attacks of tracheitis, colds and quinsy, and frequent abdominal cramps, the patient remained in poor health.

On June 25, 1943, treatment with dicumarol was started with the hope of preventing the complicating factor of thrombosis, and under continuous dicumarol treatment the patient has enjoyed remarkably active good health with no abdominal pain. The lymphocyte series has been gradually increasing since radiation but without any clinical deterioration. During the treatment with dicumarol there has been no evidence of hemorrhage in any part of the body.

JOHN E. KIRKPATRICK, M.D.

Hardy J. D., and Godfrey L. Jr.: *The Effect of Intravenous Fluids on Dehydrated Patients and on Normal Subjects*. *J. Am. M. Ass.*, 1944, 26-31.

The authors note the effect of intravenous fluids on the cardiac output, stroke volume, pulse rate, and

blood pressure of a group of dehydrated patients in comparison with similar observations made in a group of subjects not demonstrably dehydrated. Whether dehydration is the result of vomiting, diarrhea, inability to swallow, or electrolyte derangement such as occurs in diabetic acidosis, the intravenous administration of fluids is the mode of therapy usually relied on to restore the normal state of hydration and electrolyte balance. The dehydrated individuals experienced a pronounced increase in cardiac output after the infusions, while the normal subjects presented little or no such rise.

Blood was first drawn for determinations of the serum protein, serum chloride, and blood urea nitrogen. The cardiac output was calculated by the urea method and the correction of Courmand, Ranges, and Riley was employed. The technique used is described in detail. Following the readings of cardiac output, stroke volume, pulse rate, and blood pressure, 2500 cc. of intravenous fluids were administered at a rate of about 20 cc. per minute. The first liter of fluid was usually an isotonic solution of sodium chloride; the second, 5 per cent dextrose in isotonic solution of sodium chloride; and the third, 5 per cent dextrose in water. Ballistocardiograms, pulse-rate, and blood pressure readings were taken after each liter of fluid was administered.

The authors note that the cardiac output of the dehydrated group increased substantially with the administration of intravenous fluids while that of the normal group underwent no such rise. The 2500 cc. of fluid administered intravenously provoked no subjective symptoms in any of the normal subjects but it was followed by a prompt diuresis.

The normal persons had to void frequently during the infusion and the dehydrated patients did not. In the latter group more fluid was retained in the body. The fluids given intravenously doubtless increased the circulating blood volume in most of the dehydrated patients described here. Intravenous fluids may cause effects in diseased subjects very different from those observed in healthy persons.

In conclusion, the authors note that the feeling of general well-being so often experienced by the dehydrated patient after receiving fluid intravenously is accompanied by concomitant objective changes in the circulatory dynamics. The maximum effect is quite often produced by the first liter of fluid and this amount may be sufficient in such instances in which there is danger of giving too much fluid intravenously. When giving fluids intravenously to dehydrated patients, one should remain aware of the increased work which such therapy imposes on their hearts.

HENRY F. TRAUBER, M.D.

Kozoll, D. D., Popper, H., Stelgmann, F., and Volk, B. W.: *The Use of Gelatin Solutions in the Treatment of Human Shock*. *Am. J. Med. Sci.*, 1944, 908-1421.

Since human plasma or blood is not available in unlimited quantities, plasma substitutes are being

developed from macromolecular substances. The first to be used was gum acacia, which has been discarded because it is deposited in the liver. Pectin, isinglass, and gelatin have been recommended.

This study deals with the results of treatment of shock in human beings by the administration of gelatin solutions. Gelatin is a mixture of various proteins, which vary in type and molecular size in different types of gelatins according to their source and preparation. It can be prepared as a nontoxic solution isotonic to plasma and somewhat more viscous than it. Experiments on rats, rabbits and dogs at the Upjohn Research Laboratories, Kalamazoo, Michigan, have demonstrated that the gelatin solution used in these studies is well tolerated without toxic effects. The methods used in treating 52 patients are described by the authors.

In none of the patients was there any evidence of pyrogenic or other untoward reaction to the gelatin administration. No chills, abrupt rise of temperature, or complaints of pain were noted. No hemorrhagic tendencies were apparent. After the gelatin infusion, whole blood or plasma was given repeatedly without any complications. The mean of the hemoglobin, plasma density, total protein, nitrogen, and hematocrit dropped markedly after the gelatin infusion and remained below control value for twenty-four hours. The hemoglobin decreased slightly less and the total protein nitrogen significantly less than the hematocrit. The nonprotein nitrogen showed on the average an increase immediately and twenty-four hours later but it was not statistically significant because of marked deviations in both directions.

The sedimentation rate, which was markedly elevated before treatment, rose consistently the increase being statistically significant. The rise was maintained from twenty-four hours to five days. This increase in the sedimentation rate was not influenced by dextrose, saline solution, blood, or plasma given following the gelatin.

The systolic and diastolic blood pressures, which were markedly reduced before treatment, rose upon completion of the gelatin infusion and were maintained. An improvement of the pulse was observed, as well as a change in the skin from a cool and clammy condition to a warm and dry one. No change in temperature or respiration was noted. In the great majority of cases, one gelatin infusion relieved extreme as well as moderate shock without any additional therapy.

In summarizing, the authors note that the administration of gelatin to patients in shock is a safe procedure. The only undesirable effect is the effect on the erythrocytes. The increase of the sedimentation rate, which is generally found upon injection of macromolecular substances, is an important disadvantage after marked hemorrhage. In cases of shock without severe hemorrhage, no evidence was found that the increased sedimentation rate was of clinical significance. No signs of venous thrombosis were noted. Absence of a low degree of antigenicity of gelatin has been demonstrated previously as well as

the fact that gelatin is not utilized in tissues to a significant degree in contrast to other macromolecular substances. Gelatin solution is an effective blood-modulating agent. The solution of the red cells as judged from hematocrit and hemoglobin appears more marked than that of the plasma proteins. One thousand cubic centimeters of a 5 per cent gelatin in normal saline solution seemed sufficient to the authors in most cases.

In conclusion, the authors note that the results of future investigations will decide whether the nitrogen content of gelatin has nutritional value after its intravenous administration in shock, as it was found to have in experimental animals.

HENRIET F. THOMPSON, M.D.

MISCELLANEOUS

Glaser, H. Congenital Hereditary Lymphedema (Milroy's Disease). *J. Pediat.* St. Louis 1944, 5: 337.

The author reviews 2 cases of congenital, hereditary lymphedema observed at the Milwaukee Children's Hospital. The condition is extremely rare and the author is unable to find more than 50 families so affected which have been reported in the literature. In view of some very excellent reports on several generations, the hereditary tendency seems to be proved. The etiology seems to be entirely unknown and congenital malformation of the lymph vessels is widely accepted. Some possible causes are somatic disturbances, a focus or lymphatic obstruction or thrombosis.

The condition consists of a firm pitting edema affecting part of or the whole leg, or both legs, and never extending above the upper femoral ligament. There usually are no pain, attack or general inflammation.

Two and no constitutional symptoms. The edema appears to be physiological in color and texture.

The laboratory findings, including blood chemistry and counts, urinalysis, basal metabolism, the Aldrich McClure test, and x-ray pictures of the limbs are all normal. The pictures of the skin show swelling and increased trabeculation of the subcutaneous tissues with radial arrangement of the trabeculae.

The few lymphatics reported in the lymphatic enlarged spaces which may be lymphatic in origin, increase of subcutaneous tissue. The course is chronic and progressive unless treated. With treatment the edema can be reduced but it returns to its dimensions soon after regular activity is taken up and compression of the limb discontinued. Bandaging will reduce the swelling if it is done correctly, but is unsuccessful. The best results have been obtained with adhesive tape or pure rubber roller bandages. Elastic bandages and stockings as well as various boots have been tried. In later stages progressive fibrosis reduces the compression effect. The operative procedures of the type of the lymphatic operation or that of astrunk have been employed in severe cases. Other surgical procedures are the insertion of silk or of cellophane. Sympathectomy has been attempted but was considered useless.

The author reviews in detail 2 cases at the Milwaukee Children's Hospital and the treatment employed. The effect of the treatment was temporary. The histological examination of the sections of one patient proved the presence of definite tissue changes, and ruled out the possibility of the lymphatic fluid or blood. The clinical and laboratory report substantiate the fact that this is not a constitutional disorder.

HENRIET F. THOMPSON, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Sergeant, T. R. and Morton W. A.: Delayed Suture of Soft Tissue Wounds. *Lancet* Lond. 1944, 147
333

Soft-tissue wounds uncomplicated by fractures or other serious injuries constitute half of all battle casualties. The desirability of the early recovery of such a large group is obvious. In the Allied armies the accepted treatment is early débridement followed, if there is not too much skin loss by delayed suture. Early closure of the skin not only prevents infection but also decreases the fibrosis and scarring that accompany slow healing.

The importance of suturing the 'little wound' should be emphasized, particularly if the patient has no other injury often it appears insignificant and in the press of more urgent work is not given adequate consideration. With suture the wound should be healed in from seven to ten days and the patient returned to duty without suture, infection develops epithelialization is retarded and the insignificant 'little wound' takes several weeks to heal. Under ideal conditions the average rate of growth of epithelium from the wound margin is one-eighth inch a week, but infection retards this growth either along the whole margin or irregularly so that one or more areas of infected granulation tissue may persist for weeks. The longer a wound remains open with mild superficial infection the more fibrosis develops deep in it and interferes with the blood supply of the new epithelium epithelialization of the central portion of the defect is thus extremely slow and the new skin is prone to break down under the wear and tear of exercise.

The advantages of early closure of wounds cannot be denied but the decision as to when and how to close them is not always easy. To ascertain the indications for suture the authors made a survey of 143 soft tissue wounds, 100 of which were closed by delayed suture. The operations were performed by staff members of a Canadian General Hospital in the Mediterranean area during a six month period.

The wounds were from three to one hundred and thirty four days old and from $\frac{1}{4}$ inch in diameter to 9 inches long deeply involving muscle. In a sutured wound, complete healing within fourteen days was termed "success" complete healing within twenty-one days "partial success" and healing in more than twenty-one days failure. In the 100 cases there was complete healing in 53 within four ten days, partially successful healing in 20 within twenty-one days and no healing in 27 after twenty one days.

It is considered a mistake to close a wound under five days from the time of wounding since it is impossible to tell what degree of superficial infection is present, what additional necrosis may result from

the trauma of the missile, or whether a deep-seated infection or foreign body reaction will develop.

If no contraindications are evident after five days have elapsed the wound should be sutured as soon as possible. In the first nine days the walls of the wound are soft and pliable and can be easily approximated provided there is not too much loss of tissue. Between the eleventh and fifteenth days granulation tissue appears on the floor of the wound and a thin bluish line of new epithelium can be seen growing from the skin margins. This means that the walls have already lost much of their pliability the skin margins have become adherent to the granulation tissue on the floor and approximation may necessitate additional surgery such as undercutting of the margins.

The wounds which healed best had undergone early débridement consisting in minimal excision of the skin adequate exposure of the depths excision of all the damaged soft tissues and removal of all the foreign material. The cleanest wounds were those covered by a very light plaster-of Paris cast.

Cultures taken from the 100 wounds (79 of those that were subsequently sutured and 21 of the unsutured) showed that the staphylococcus aureus was the commonest offender the streptococcus haemolyticus coming next the latter however was not prominent until after twenty-one days. Up to ten days only single strains of bacteria were found, the combinations seen later almost always included the staphylococcus aureus with a diptheroid. Criteria for the suture of wounds should be based upon the clinical appearance not on the bacteriological findings.

After from five to nine days a débrided wound which is suitable for suture should show the surrounding tissues to be normal on palpation not indurated and not tender and the skin margins should show no reaction. If tenderness, reddening of the skin margins purulent discharge or necrotic tags of muscle, fat, or skin are present, suture is inadvisable.

Wounds from ten to twenty-one days old which are suitable for suture should show no sign of induration or tenderness, and the skin should be soft and pliable up to the very margin of the wound.

Before suture of wounds over twenty-one days old is done the surrounding skin should be pliable. A shelving margin with a growing border of new epithelium should be present. The base should be covered by smooth granular beefy red granulation tissue, and the exudate should no more than faintly stain gauze kept on the wound for twelve hours.

Dry gauze applied with firm pressure is the best postoperative dressing. Immobilization by plaster of Paris splints may be necessary.

Failures were commoner with wounds on the anterior surface of the leg the lateral aspect of the thigh and greater trochanter the upper medial por

tions of the buttocks and on the back. The factors concerned appeared to be tightness of the skin tension of the deep fascia, inability to immobilize the part completely and difficulty in preventing the patient from lying on the wound.

The antiseptic treatment which seemed most successful was the use of 1:4 eusol solution until the purulent exudate had diminished, then a change to 5 per cent saline solution and finally alternation of these solutions every few days.

Approximately two-thirds of the wounds were influenced with a sulfonamide powder at the time of the delayed suture and one third were not. Suture of wounds over ten days old was not appreciably affected by this treatment. For the wounds from five to nine days old however the sulfonamide powders seem to have been beneficial. It seemed expedient to emphasize that the local use of sulfonamide can never be anything but an adjunct to good surgery.

STEPHEN A. ZILMAN, M.D.

Rogers, L. S.: Abdominal Surgery In Forward Areas: Observations Made In A Casualty-Clearing Station, 1941-1942. *Austral N Zealand J Surg* 944, 4 37

The place best suited for abdominal surgery is the casualty-clearing station separate resuscitation units working in advance of this station would only delay the arrival of the patient to the abdominal surgeon. The chief resuscitation ward is the preoperative ward of a casualty-clearing station. The x-ray plant is placed at the distal end of the preoperative ward in every case of penetrating wound of chest, buttock and upper thigh an x-ray examination in one plane is carried out as a routine. Two planes are used only in difficult cases.

If under resuscitative measures (sedation, blood transfusion, warmth) the patient improves and says that he feels better operation is delayed until the diastolic pressure reaches 80 and the systolic 100. If there is no improvement, immediate operation is undertaken, after 5 pints of blood have been given to stop the internal hemorrhage. The time factor of itself does not preclude operation. Patients whose condition is three days old have been saved.

The incision varies with the condition found or anticipated, once an opening has been made into the abdomen, however, all free fluid is rapidly aspirated also that in the pelvis. Control of the bleeding is undertaken first, if it is coming from the spleen splenectomy is done, otherwise, undersewing with mattress sutures is done. All holes into the chest cavity are closed first. In exploration the start is made in the large intestine. If a hole is found lateral mobilization and exteriorization of the part is in order. Next the ileocecal junction and the small intestine and stomach are explored, thoroughly and rapidly each hole being clamped with a Poirier forceps. Finally the bladder is inspected. Repair is always better than resection when it is possible. End-to-end junction after resection is best for the small intestine. Simple suture is done. A Miller

Abbot tube should be guided through the pylorus at the end of the operation. In wounds of the rectum, bladder and sigmoid colon the Trendelenburg position is used only after the pelvis has been aspirated. The pelvis should be drained after every perforating wound. Blood collection in the area often means a pelvic abscess later. The pelvic drain should be clamped when the operation is finished. Sulfadiazine emulsion is injected, and this is then washed into the abdominal cavity by a further injection of 30 cc. of sterile saline solution.

Postoperative treatment begins at once in all abdominal cases with continuous gastric lavage and suction. The nasal route is the best. With the tube in place the patient is allowed to drink whenever he feels like it. Three times a day the stomach tube is disconnected, and 500 cc. of hot sodium-bicarbonate solution are injected. Lavage and suction are maintained until intestinal movements are continually heard and flatus and feces are passed. Fluid balance is carefully watched. Fluids are given parenterally for the first two or three days, then a continuous rectal drip. Flatus competitions are encouraged. Morphine in doses of $\frac{3}{4}$ gr every four hours and $\frac{1}{4}$ gr at night is given continually for the first two days (sleep and rest to the bowel are necessary). The abdomen is inspected twice a day and hot copious bowel washouts with postural treatment are begun the moment distention appears. When intestinal movements are heard continually and flatus is being passed, the stomach tube is clamped and fluids are allowed by mouth. If there is no residue at the end of four hours, the tube may be removed. If vomiting occurs the tube is reinserted immediately.

Sulfathiazole is given intravenously while suction continues. A second dose of sulfadiazine emulsion injected down the pelvic tube has been found to cause intense pain and dysuria for twenty-four hours it has therefore been given up.

Danger signs in abdominal cases are these: persistent hiccup which starts even during operation; slow persistent distention with a silent abdomen; continual anxiety and a high pulse rate and diminution of the urinary output. In retroperitoneal wounds distention starts very early and is progressive. Stomach suction is not usually sufficient to deal with the ileus. Semi-erect position of the penis is often present and is a bad sign. In these wounds the prognosis is usually bad. JOHN W. BARNARD, M.D.

Macdonald: Observations on Battle-Casualty Compound Fractures and Joint Injuries in the Middle East. *N Zealand M J* 944, 43 7

Macdonald describes his experiences as an orthopedic surgeon with a New Zealand hospital unit in the Middle East during 1941-1942 and part of 1943, especially in regard to battle-casualty compound fractures and joint injuries. It must be understood that continuity of treatment by any one man of any one serious long-distance case seldom occurred.

The author is emphatic in stating that primary skin suture holds no place at all in front line surgery.

(as it occurred in the Western Desert) It became standard technique to carry out simple surgical toilet of the wound followed by the insufflation of 10 gm of sulfanilamide and the application of vaseline gauze without suture of the skin edges. He condemns the use of the vaseline plug as it was found that many wounds were packed too tightly and too voluminously. He recommends that a minimum amount of vaseline gauze be used, enough only to keep the wound edges gently open. Débridement as we know it was not practiced. It was found sufficient to remove only the obviously devitalized tissue and to open up for drainage any of the deeper spaces which might have become infected and then have pocketed.

The Thomas Splint, if it ever needed vindication has certainly received it in the Middle East. Macdonald states that all patients with femur and knee-joint injuries on whom the splint was correctly applied, traveled more comfortably and arrived in better condition than did those which were put in plaster. The Tobruk plaster (Thomas splints with added plaster-of-Paris) came out of this campaign. The badly fractured humerus was put up in treble V shaped plaster, the elbow at 90 degrees, the forearm in neutral rotation and the whole unit then bound across the front of the chest. Knee joints were treated on Thomas splints with fixed skin traction.

The author concludes by stating that the factors responsible for the good results were massive transfusions, sulfanilamide, infrequent dressings, avoidance of primary skin suture, efficient splinting, recognition of the fact that the first operation is the one which counts, and sending the surgeon to the patient rather than sending the patient back to the surgeon.

J. M. Moxa, M.D.

Churchill, E. D. The Surgical Management of the Wounded in the Mediterranean Theater at the Time of the Fall of Rome. *Ann. Surg.* 1944, 120: 268.

Foreword by Brig. General Fred W. Rankin, M.C. As Surgical Consultant to the North African and Mediterranean Theater of Operations and representative of this group, Colonel Churchill has done more than improve the quality of surgery performed in this Theater. Uniquely equipped to perform his mission and imbued with the true scientific spirit, he early recognized the inadequacy of certain preformed concepts in the surgical management of the wounded. With this flexibility of mind and with an elastic organization, he has utilized an investigative approach and drawn upon battlefield experience to evolve more rational and effective methods in the surgical care of the wounded. In this article, he has epitomized these observations and principles which constitute not only a contribution to war surgery but also to the advancement of medical science.

The surgery of warfare is divided into three phases of management. The initial and reparative phases of wound treatment are given overseas; the recon-

structive phase is administered in the zone of the interior.

INITIAL SURGERY

Initial surgery in the battle area is intended to preserve life and limb by correcting the abnormal physiology resulting from the loss of blood and other body fluids. Included in the procedure are resuscitation and chemotherapy for the limitation and restriction of infection. Resuscitation makes possible the transportation of the casualty and permits him to withstand essential surgical operations. In the divisional forward areas, plasma is used. However, after admission to the hospital, it is replaced by whole blood which is procured and processed by special units. Over a four month period, 16,000 pints of blood were delivered to the Fifth Army on the Anzio beachhead. Only Type O blood (universal donor) with an agglutinin titer below 64 and a seven-day expiration date was used. Other types of blood are maintained by unit blood banks in evacuation hospitals. The prevention of infection is attempted by means of débridement of the wound. Oftentimes it is impossible to recognize all devitalized tissue. Therefore, primary closure by wound suture is not performed. Only provisional or temporary fixation of fractures is performed because of the necessity of evacuation. The value of local sulfonamide chemotherapy is questionable. However, penicillin therapy is administered to all battle casualties except the slightly injured. Topically, it is used only in the meninges, serous cavities, and joints. Parenterally, it is continued beyond the expected period of infection. However, chemotherapeutic agents cannot be expected to prevent septic decomposition or render sterile any devitalized or avascular tissue. Nevertheless, penicillin has enlarged the scope of military surgery and opened vast new fields in wound management.

Initial surgery is not hasty, slap-dash surgery, but really precision surgery of a highly specialized type. It often involves the treatment of multiple serious wounds that require the co-ordination of surgical specialties. At the divisional clearing station, first priority cases are evacuated for treatment to a nearby first priority surgical hospital. These hospitals are manned by highly trained and experienced personnel comprising an Auxiliary Surgical Group.

REPARATIVE SURGERY

As a result of the use of penicillin, reparative surgery at the base hospitals has been completely revolutionized in every surgical specialty. It must be distinguished from reconstructive surgery, which is a function of hospitals in the zone of the interior. At these base hospitals, at least 25,000 wounds were closed by suture with healing in 95 per cent and no loss of life or limb. Wounds are closed by secondary suture as early as the fourth day after injury solely on appraisal of the gross appearance of the tissues after removal of the evacuation hospital dressing. Qualitative or quantitative bacteriologic analyses of

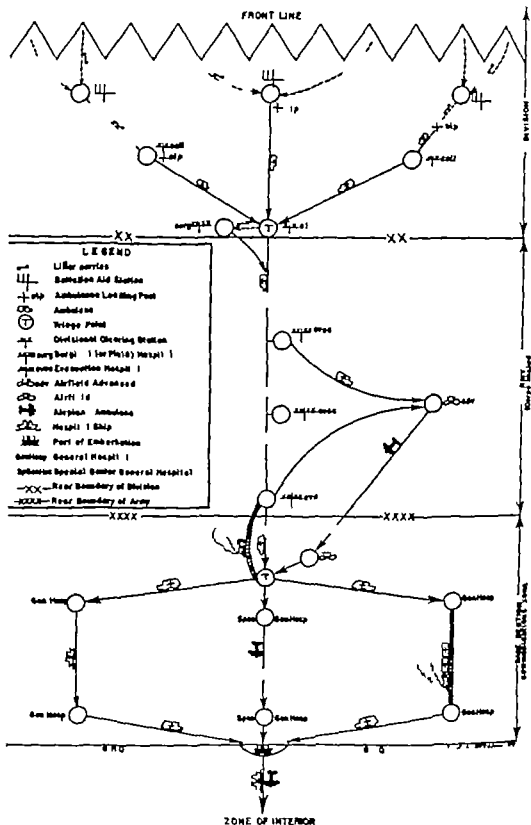


Fig. 1. Diagrammatic representation of an overseas theater (Courtesy of J. B. Lippincott Co.)

wound cultures are of no special value since many wounds have been found to heal by primary intention even in the presence of a profuse and varied flora. The most common cause of failure of secondary suture was due to infection caused by residual dead tissue. This may be detected at the first dressing by the discharge of pus and the inflammatory appearance of the wound margins.

Complicated wounds involving the soft parts and bony structures are the cause of the major part of reparative surgery. Compound fractures coming to base hospitals are removed from the transportation splints the wound is revised, and the fracture is reduced. In this group of patients the continuous penicillin therapy from the inception of wounding through to the evacuation to the base hospital has been of great value. Combined with whole-blood transfusions for anemia it has made possible reparative operations of the greatest magnitude and enabled the closure of original débridement incisions of compound fractures. Wounds of joints are treated by arthrotomy with the removal of devitalized cartilage and foreign bodies, after which the joint space is closed. In a severely traumatized joint, it may be even resected.

Massive organizing hemothorax is treated by thoracotomy, evacuation of the clot, and decortication of the lung. Post-traumatic empyema of the lung treated by surgery in combination with penicillin has resulted in rapid repair with full expansion of the lung. Advances in thoracic surgery have been such as to make possible the preservation of the maximum amount of lung tissue.

Skin grafts may be performed as early as the fourth day after injury. Primary suture of facial lacerations with splinting of the bony parts plus control of infection has resulted in a marked reduction of disfiguring mutilations. Early repair of intestinal fistulas and exteriorized segments of large bowel is performed at the base hospital with significant advantage. At this type of installation, cranio-cerebral wounds are closed and now even injuries of the peripheral nerve are repaired early.

Reparative surgery constitutes a new concept in military surgery. Just as the time-lag between wounding and initial surgery is related to the preservation of life and limb, so does the interval between initial and reparative surgery offer golden opportunities for adding to the preservation of life and limb.

BENJAMIN G. P. SHAPIROFF, M.D.

OPERATIVE SURGERY AND TECHNIQUE POSTOPERATIVE TREATMENT

La Roa, E.: Breast Tissue as a New Source for Heterogenous Implants. *Am. J. Surg.* 1944 66 38.

Fresh and preserved breast tissues are used as implants in plastic work. The first breast tissue was secured from pendulous breasts. The donor patient and the recipient had the same blood grouping. The sedimentation rate, coagulation time and hemo-

globin were within normal limits. The erythrocytes, leucocytes and differential count were well within normal limits. The breast tissue upon removal was placed in a saline solution and kept warm.

Immediately after removal of the breast tissue the recipient patient was surgically prepared and the defect caused by an amputation for a scirrhus cancer was prepared for the transplant. The transplant was patterned to approximate a normal breast and was sutured into position. The temperature of the patient was slightly elevated following the operation. On the eighth postoperative day there was a bloody discharge from the breast dressings. The hospital stay was sixteen days. On the twenty-ninth day there was a recurrence of the sanguineous and fatty discharge. Four fifths of the original transplant remained. About sixty days postoperatively an additional sloughing occurred which lasted for ten days.

The breast tissue which was not used in this first operation was transferred to a sterile Tyrode solution and kept at a temperature of 45° F. Bacteriological tests were carried out periodically. On the seventh day portions of the preserved breast tissue were used in 3 operations. In the first, a portion was implanted in a defect of the forehead due to injury. This patient was discharged from the hospital on the third day. There was a primary healing on the seventh day. The end result, at three months appeared to be permanent.

In the second case a portion of the preserved breast tissue was implanted to correct a deformity of the nose. The end-result appears to be satisfactory.

The steps in the preservation of the tissue in Tyrode solution are enumerated. The Tyrode modification and the preservation of human tissue appear to be satisfactory.

RICHARD J. BENNETT, JR., M.D.

Harris, H. I.: Heterogenous Skin Grafts by the Coagulum-Contact Method. *Am. J. Surg.* 1944 65 315.

The author stimulated by the works of Sano reports the successful use of the coagulum-contact method for heterogenous skin grafts in 9 instances.

The histological changes on the application of a graft to the donor area are divided by Fomon into three stages: (1) the stage of plasmic circulation, (2) the stage of vascularization, and (3) the stage of organic union. The coagulum-contact method replaces the stages through which the tissue must pass in order to arrive at the same goal, and saves a period of from twenty-four to forty-eight hours. By the use of this contact method many hazards are eliminated. Shock is lessened by shortening the duration of the operative procedure and by lessening the quantity of anesthetic used.

The author paints the cell extract on the graft while it is still on the drum when the Padgett machines are used. In free hand grafts and in full thickness grafts the graft must be placed upon some material such as gauze. Complete hemostasis must be accomplished in all cases before the grafts are

applied. In redressing patients, the author uses a warm saline pack or compress for a few minutes before reapplying the dressing.

HAROLD C. OCHSNER, M D

Elman, R.: Acute Starvation Following Operation or Injury with Special Reference to Caloric and Protein Needs. *Ann. Surg.* 1944, 120, 350.

Six nutritional elements water salt, protein fat, carbohydrate and vitamins must be considered in discussing starvation.

In surgical practice measures are taken to prevent water and electrolyte starvation particularly by the simple injection of physiological saline solution. In addition most patients receive a certain amount of carbohydrate, sufficient at least to prevent ketosis although usually insufficient to meet all of the caloric needs. Vitamins, neglected for a great many years now are given adequately even if the patient is unable to take any by mouth. The remaining elements are fat and protein.

Deprivation of protein and caloric needs wholly or partially, although frequent, is, in general, viewed with complacency or considered inevitable. The supposition that tissue and other stores will supply safely the needs of the body has produced deleterious results. Wastage of body tissue, particularly tissue and plasma protein is not without untoward effects which begin almost at once after protein is removed from the diet.

When a healthy well nourished individual sustains a serious injury or undergoes a severe operation, starvation nearly always ensues. While the causes of such starvation are those which lead to deprivation of one or more of the nutritional elements, as a result of the injury there follows an unusually large breakdown of protein tissue, the toxic destruction of protein which leads to protein depletion even with the intake of a normal well balanced diet.

Even though the food requirements are normal and the patient is able to eat, the dietary intake after injury or operation is nearly always inadequate because of the starvation imposed by the surgeon who fears that the ingestion of food will prove deleterious. Often only fruit juices and broth are permitted such an intake leads to electrolyte or protein starvation or both. Excluding patients in whom it is necessary to keep the gastrointestinal tract at rest, as in general peritonitis, or in whom vomiting is present, such fear is usually without foundation. On the other hand when the patient cannot eat or is vomiting protein starvation will ensue because the usual parenteral injections contain only electrolytes and glucose.

Starvation in other patients may be due to partial or complete loss of appetite following the injury or operation aggravated often by overmedication particularly with morphine. Thus, there follows a failure in the normal impulses which ordinarily insure an adequate intake of food, and the patient left to his own resources does not eat, even when perfectly

adequate trays of food are served. Ordinarily anorexia ends quickly and spontaneously and the patient soon begins to eat of his own accord however, in many cases anorexia persists and becomes a manifestation of starvation itself. Thus a vicious cycle is established by which the very effect of starvation becomes a further cause.

The effects of acute starvation after injury or operation are

1. Loss of weight which, if water balance is maintained or its influence taken into account, means loss of body tissue but its physiological significance depends upon which of the two body tissues, fatty or protein, is depleted. Loss of protein tissue can be measured clinically by the amount of nitrogen excreted largely as urea and ammonia. Studies have shown that after injury or operation, as much as from 20 to 40 gm. of nitrogen may be excreted per day. By contrast, loss of fatty tissue, even if all of 2,000 calories were supplied by fat, would represent only 100 gm., or in terms of the tissue itself, 140 gm or one half pound, a day.

2. Asthenia. Most of the postoperative weakness or asthenia is attributed by surgeons to the operative procedure, but it may actually be due to starvation, particularly deprivation of protein. It has been shown that normal human beings who ingested a diet complete in all elements except protein developed after forty-eight hours severe symptoms of lassitude and asthenia, which were corrected rapidly by the ingestion of protein food. Elman has often observed that postoperative weakness was decreased by the intravenous injection of hydrolyzed protein. Jejunal alimentation beginning immediately after operation alleviates most of the asthenia symptoms and, in addition, accelerates convalescence.

3. Nutritional edema is an important serious clinical manifestation of starvation and may involve the gastrointestinal mucosa. Moreover it may be responsible for delay in wound healing, anuria, and even circulatory impairment. All of these complications may follow severe injury and operation, and, besides certain physical factors, hypoproteinemias long has been recognized as the most significant cause of nutritional edema.

4. Lowered resistance to infection is demonstrated by the fact that the production of antibodies is but from one-third to one-fifth as great in protein-deficient animals with hypoproteinemias as in animals on a regular diet, and it is probable that many postoperative infections may be due in part to a lowering of the immunological response of the body secondary to protein starvation.

5. Hypoproteinemias frequently occurs after operation or injury. Although published data on the extent vary considerably hypoproteinemias frequently escapes detection because its existence is masked by two factors (1) the albumin fraction which is obscured by an increase in the globulin fraction due to the infection and (2) dehydration, which is responsible for a normal concentration of both fractions, although the total circulating protein is depleted.

6. Death That a fatal outcome after injury or operation may be due to starvation is an inescapable conclusion in several instances. Extreme emaciation is always the prominent finding at postmortem examination.

Treatment of starvation is simple, consisting merely of overcoming the patient's loss of appetite with adequate food intake, looking to the palatability of the food and avoiding idiosyncrasies making judicious use of sedation and giving a diet complete particularly in adequate protein.

Three glasses of a drink made by stirring 100 gm of skimmed milk powder into 200 cc. of water furnished 34 gm. of protein and 52 gm. of carbohydrate. These amounts exceed those in a quart of milk with only one fifth of its volume, and will meet the daily protein needs of a normal-sized adult. Solid food such as eggs and meat should be added as soon as possible. If necessary parenteral or tube feeding after operation or injury may be employed. The bulk problem can be made easier by sacrificing some and perhaps even a considerable part of the caloric requirements.

Evidence indicates that a large part of the caloric needs may safely be sacrificed for short periods with out physiological impairment provided an adequate protein intake is assured.

It may be more important to insure nitrogen balance with a high protein diet than to provide fat and carbohydrate for all the caloric needs. Should loss of body weight occur as a result of starvation it is much more important that nonessential tissue fat rather than essential tissue and plasma protein be depleted.

Starvation may be avoided to a considerable extent by recognizing anorexia as a therapeutic challenge rather than an inevitable symptom. Because prevention of starvation is much easier than its cure adequate nutrition should begin immediately after injury or operation. STEPHEN A. ZICKMAN M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Orr Ewing, J. Scott J. C. Maalaa, F. H. Trueta, J., and Gardner, A. D.: Local Sulfanilamide Treatment of Fresh Wounds In Complete Plasters. *Brit J Surg* 1944 32 83

This investigation was aimed at obtaining incontrovertible evidence about the effect of local application of sulfanilamide on the bacteriological condition of compound fractures and other severe wounds treated by thorough cleaning, excision and enclosure in plaster and at correlating this evidence with the clinical results. The authors treated a series of cases with and without the local application of sulfanilamide, attempting to avoid any selection that might vitiate their conclusions.

They demonstrated a selective reduction of the wound flora by sulfanilamide but did not establish a corresponding clinical effect.

HOWARD A. MCKNIGHT M.D.

Connor G. J. and Harvey S. C. The Healing of Deep Thermal Burns. A Preliminary Report. *Ann Surg* 1944 120 362

The chief cause of delay in the healing of deep thermal burns is the continued presence of the slough. Dead tissue is essentially powerless to combat infection as long as it is present. Successful skin grafting is impossible, and contracture continues hence the advantage of removal is fully realized.

Enzymatic digestion of slough in wounds has been tried with a proteolytic compound containing papain, urea and caroid in a saturated aqueous solution and various other enzymatic compounds. Several of these however damage living tissue.

The hydrogen ion concentration of the wound fluid is increased in many infected wounds and preliminary experiments with local application of various organic and inorganic acids revealed that the separation of the slough could be greatly hastened if the pH of the surface of the wound was sufficiently lowered. Of the large series of acids studied pyruvic acid presented outstanding advantages. With it the necessary balance between the pH and concentration of the acid can be obtained in order to accomplish the desired results.

Deep burns produced on dogs by the direct application of a low blue gas flame to the skin for twenty seconds over the dorsolateral aspect of the trunk resulted in a standard burn from 3 to 4 cm. in diameter and uniformly involved the full thickness of the skin.

The experimental wounds were dressed within a few hours after burning with a thick layer of paste consisting of a solution of pyruvic acid at a pH of 1.0 and of 8 per cent cornstarch.

The control wounds were dressed within a few hours after burning with either dry gauze, vaselined gauze or a paste consisting of 8 per cent cornstarch in distilled water.

In the experimental series the slough separated completely within seventy two hours whereas in the control group the complete separation of the slough required from ten to twelve days. The slough softens on its surface and breaks up into many pieces which are firmly adherent. During the week before complete separation the wound is covered with a necrotic, stringy adherent layer.

The separation of the slough in the experimental group however appears to begin at the periphery where, in twenty four to thirty-six hours there is slight softening. A plane of cleavage develops beneath the otherwise intact slough and separation proceeds centralward. After forty-eight hours the cleavage has developed to the point where the slough, aside from soft dermal tags at the periphery is either completely free or loosely attached beneath its center. In another twelve to twenty four hours separation is complete with the slough lying free in one piece.

There is no evidence of digestion of the slough itself and the skin adjacent to the burn appears undamaged.

Grossly, the resultant base is pink subcutaneous tissue. Within seventy-two hours after burning this base is unusually vascular and, histologically exhibits evidence of early granulation tissue. The edges of the wound are sharp and clean and are often tangential as would be consistent with the more superficial damage at the very margins. The pink clean base evident after separation of the slough accepts a split graft of skin immediately. This regularly takes, and all or part of the wound may be successfully treated in this manner.

The problem of infection is thus resolved and the full objective of treatment achieved, even before the slough in the comparable control wound has completely separated.

The use of this method on man is being studied but has not as yet been adequately tested, nor has a standardized procedure in all details been adopted. Until these have been done, application of the method for the purposes of treatment should be delayed.

STEPHEN A. ZIDMAN, M.D.

McClure, R. D., Lam, C. R., and Romance II.: Tannic Acid and the Treatment of Burns. *An Obsequy Ann. Surg.* 1944, 80: 387.

Twenty years ago the tannic acid therapy of burns was begun at the Henry Ford Hospital. The authors of this article hope that this communication from a group working in the same institution will result in the abandonment of this type of treatment of burns and related methods. This unqualified recommendation is prompted by comparatively recent clinical experience and animal experiments by the authors and others. Under certain circumstances the use of tannic acid produces a severe if not a fatal lesion in the liver and carefully controlled experiments have shown that it moderately inhibits wound healing.

Four illustrative cases are reviewed. Two cases were treated with tannic acid and 2 were treated with presumably inert vaseline dressings. Liver necrosis and jaundice were present only in the tanned cases.

The authors raise the questions: If tannic acid is toxic to the liver and does local damage, why was it used for 20 years and why was it adopted so enthusiastically almost all over the world? What about the much publicized mortality rate reductions? We fear that the largest factor was wishful thinking.

Liver necrosis has been reported in a considerable number of burned patients treated with tannic acid. Nonfatal cases frequently show marked disturbance of liver function in the acute phase of the burn. The liver lesion is easily reproduced experimentally. Wound healing experiments on animals and on human donor sites indicate that tannic acid retards healing considerably.

JOSEPH GARTER, M.D.

Jackson, A. V.: Liver Necrosis in Burns Treated with Tannic Acid. *Med. J. Australia* 1944, 352.

Since the outbreak of war the tannic-acid method of treatment of burns has been criticized from sev-

eral points of view. It appears to be unsuitable for certain areas, such as the face and hands, because the rigid eschar is sometimes followed by ischemia. Also trouble is sometimes caused by sepsis hidden under the eschar. Of even more serious import is the suggestion, first made in 1943 by Wells, Humphrey and Coll, that tannic acid may cause liver necrosis.

It appears from the review of the literature that pronounced liver necrosis is common in patients who die from burns treated with tannic acid, and is slight or absent from those not so treated. However, the two groups—the tannic-acid group and the nontannic-acid group—are not quite comparable. Nearly all the patients not treated with tannic acid died before 1935 so that not only did they not have tannic acid treatment, but they also did not have the benefit of modern ideas regarding the importance of hemoconcentration in burns and its control by intravenous serum therapy nor were modern chemotherapeutic agents for the control of sepsis available. Consequently, the older patients frequently died in the first three days from septicemia, or after the eleventh day from sepsis.

In spite of the accumulating evidence to the contrary, therefore, it still remains a possibility that the failure to observe liver necrosis in patients who were not treated with tannic acid may have been due to the fact that most of these patients died (1) before liver necrosis (caused for sake of argument, by some hypothetical burn toxin) and not by tannic acid had time to develop (2) later from septic infection of a burn not sufficiently large to cause much toxemia or (3) perhaps after liver repair had been effected.

The need of further evidence of the toxicity of tannic acid in human beings prompted the author to examine the livers of 8 patients who died from burns. All patients, except 1, died between the third and eleventh days. In the livers from 3 patients treated with tannic acid and silver nitrate, extensive hepatic necrosis was found. In the livers from patients whose burns were not treated by tanning, cloudy swelling was the only abnormality found.

JOSEPH K. NALAT, M.D.

Osborne, R. P.: The Treatment of Burns and Wounds with Skin Loss by the Envelope Method. *Brit. J. Surg.* 1944, 3: 24.

Thirty-one cases of burns were treated during a nine-month period. Six were recent burns, 13 on unhealed wounds and 12 were old burns.

Envelopes of the Bunyan-Stannard type were used, the envelopes being sterilized previous to use.

An anesthetic usually is given with the application of the first envelope. Application of the envelope consists of arranging a rubber sheet beneath the area to be treated so that the overflow runs into a receptacle. Previous dressings are removed, the wound photographed, and a smear taken for bacteriological examination. An irrigation with 1 per cent sodium hypochlorite at 110 degrees is carried out and the

the sterilized envelope is applied. The same solution is used for irrigation through the envelope. Five pints are used for an extremity. The envelope is allowed to drain for from five to ten minutes, then the interior is dried by air blown through with an electric hair dryer. Subsequent irrigations are carried out three or four times a day. Irrigation is ordinarily painless. When a smarting sensation is reduced the concentration of the solution is reduced.

Dermatitis in the form of furunculosis may be seen on undamaged skin within the envelope after two or three days; possibly it is due to insufficient drying.

Excess granulations are controlled by pressure dressings. Spints may be applied outside of the envelope if necessary. Active movements are carried out from the start. Delayed healing occasionally occurs but is accelerated by the removal of the envelope. The life of an envelope is usually from three to five weeks. Sometimes the regenerated epithelium is quite fragile and it is necessary to do a skin grafting. Skin grafting of the Thiersch type may be carried out safely after hemolytic streptococci have been eliminated; this being determined by three successive negative reports. Grafts are applied in sheets or the chessboard variety is used. The chessboard type is obtained by cutting the skin in $\frac{1}{4}$ inch squares. These $\frac{1}{4}$ inch squares are then applied to make the chessboard pattern. The envelope and a pressure dressing are then applied. Pressure dressings are removed on the third day. Irrigation (1 to 20) is carried out twice daily. There are no dressings after the seventh day.

Several of the cases are discussed in detail as to the condition on admission, treatment and bacteriology. The improvement of the patients' condition and the maintenance of full function in every case is very noteworthy. Risk of infection and crossinfection are avoided by this method.

When bacteriological examination showed the presence of the hemolytic streptococcus at the time of the application of the envelope, all of these organisms disappeared although in some cases sulfanilamide was required.

No cases of deformity occurred when the envelope method of treatment was used.

RICHARD J. BENNETT, JR.

Clarkson, P.: Late Closure of Wounds. *Lancet* Lond. 1944, 247, 395.

Late wounds are best closed by a radical attack which, by excision of granulations, the fibrotic base, and the new skin back to good surgical material, aims at reconstitution of the original defect in a clean field. This defect is then closed at the same operation.

Closure of the local tissue is possible in most of these wounds and closure in as straight a line as possible gives the best functional results and earliest sound healing.

Direct approximation and secondary suture, after wide undermining is the most widely applicable

method (40 per cent in this series) but more distant tissue may be made available by transferring it over the defect on a swing or rotation flap in a good percentage of cases (33 per cent of this series).

The upper limit of these local closures in the trunk, and proximal parts of the limbs lies between 80 and 100 sq. cm. and depends on the site of the defect. Defects of 80 sq. cm. in the elbow or upper regions of the calf can be closed by local tissue with rotation flaps and abdominal and flank tissue up to 200 sq. cm. can be made available for trunk defects.

There is no contraindication to a free graft if it will take but earlier and sounder healing is obtained when local tissue can be made to close the wound. A wound more than from six to eight weeks old does not offer a good prospect for 100 per cent take and sound healing of the graft. A free graft is nearly always necessary at least in part, for defects of more than 120 sq. cm. In such large defects the free graft can often with advantage be combined with a local flap to provide both a skin and fat cover for special parts of the wound.

With increasing use of delayed primary suture and early secondary suture, combined with local penicillin, the percentage of wounds needing late closure may be expected to decline sharply.

Soft tissue wounds however extensive should all be soundly healed within six weeks of the injury. The surgeon must be able to achieve this for his cases or else should send them early to a center equipped to do so.

JOHN J. MALONEY, M.D.

Lockwood, J. S., White, W. L. and Murphy, F. D.: The Use of Penicillin in Surgical Infections. *Ann. Surg.* 1944, 120, 311.

This article presents the experiences and results of penicillin therapy in surgical infections. It portrays what has been learned by one of the participating groups of investigators working under the program of the Subcommittee on Infected Wounds and Burns of the National Research Council regarding the scope and limitation of penicillin in surgical infections. It brings out moreover the extent to which penicillin gives promise of meeting some important deficiencies of the sulfonamides through its effectiveness in the presence of pus, its powerful action against staphylococci, and its lack of toxicity.

A brief review of the history of penicillin and its properties as a chemotherapeutic agent is given. The organisms against which it is effective and those which are resistant are enumerated.

The local use of penicillin either by itself or in conjunction with systemic therapy has given results which are highly encouraging. Emphasis is properly placed on the necessity for careful bacteriological study of every case in which the drug is used in order to determine whether or not the causative organism is susceptible or whether resistant strains of staphylococci or streptococci will be encountered which will require more intensive treatment.

Within eighteen months about 440 patients have been treated. The diseases encountered were of

many varieties, both medical and surgical, and except for special research cases of chronic osteomyelitis and pulmonary suppuration all of the patients were critically ill. Moreover most of them had received intensive sulfonamide treatment without success for periods of from two days to several weeks.

Four main groups of cases are discussed: acute disseminated sepsis, and localized infections of the serous cavities, soft tissues and bone respectively.

1. Among the cases of acute disseminated sepsis (bacteria and meningitis) there were 57 patients with staphylococcal bacteremia, two-thirds of whom survived; 15 with streptococcal bacteremia and 50 with suppurative meningitis; 43 pneumococcal and 5 staphylococcal. The patients with staphylococcal bacteremia probably illustrate better than any others the important position of penicillin as a chemotherapeutic agent. Whenever possible they were treated by the continuous intravenous drip method and received doses of from 60,000 to 150,000 units in each twenty four hour period. With impressive regularity these patients tended to show improvement within forty-eight hours and unless complications had developed, were clinically recovered from the acute disease within three to seven days. The complication most likely to interfere with successful treatment was vegetative endocarditis which developed in 10 cases. In most of these cases of bacteremia no resort was made to surgical treatment of the foci of infection during the acute septic phase, because in the face of progressive improvement in the patient's condition it seemed wise to defer operative procedures until a time of election. In several instances the foci subsided without drainage, particularly those developing in well vascularized tissues about the face and in the lung. When localization occurred in bone it was usually necessary to resort to surgical drainage ultimately.

Cases of meningitis, with or without bacteremia, particularly those due to staphylococci, have responded promptly at times even without intrathecal treatment but in pneumococcal meningitis a daily injection of about 10,000 units of penicillin into the lumbar spinal canal, cisterna, or ventricles is imperative and recent experiences suggest that the cisterna objections are particularly advantageous in severe infections. In meningitis it remains a matter of great importance to explore potentially infected mastoids when a prompt clinical response is not forthcoming.

2. Under localized infection in serous cavities are discussed empyema, suppurative arthritis, and peritonitis. When empyema is due to an infection with a penicillin-sensitive pneumococcus, staphylococcus, or streptococcus in pure culture and treatment is instituted within the first few weeks it is possible to bring about sterilization of the cavity and ultimate cure, without resort to thoracotomy drainage. Frequent aspiration of the cavity and injection of from 10,000 to 25,000 units of the drug rapidly brings about sterilization of the cavity.

In the acutely ill, systemic treatment in combination with local injection is given.

Complete restoration of function has occurred in staphylococcal arthritis, and in cases of primary peritonitis from hemolytic streptococci or pneumococci the infection would be expected to respond favorably to penicillin treatment. Less certain, however, would be the results of treatment of infection developing after appendicitis, including pyelitis and perihaptic infection.

3. Under "localized infections in soft tissues" are discussed such topics as cellulitis of the face and orbit, boils and carbuncles, and pulmonary suppuration. Particularly striking have been the results of treatment in patients with cellulitis of the face and periorbital tissues. The recuperative power of these well vascularized areas is illustrated by the frequency with which penicillin treatment has been sufficiently effective to prevent suppuration in case of facial cellulitis.

There is every reason to believe that the management of boils and carbuncles will be improved by combining penicillin therapy with surgical removal of devitalized skin, fat, and fascia. The spread of cellulitis and localization of the suppurative focus usually occurs within two or three days after systemic therapy is started.

The treatment of patients with chronic post-lung abscesses has not yielded striking results, perhaps because many of the bacteria in these lesions are resistant to penicillin. The most that can be reasonably expected of the drug in these cases is to improve the condition of the patient for operation and to reduce the incidence of postoperative infection of the pleural cavity.

Penicillin cannot be expected to have a lasting curative effect in chronic bronchiectasis, but it can be used as a means of preparing septic cases for surgical treatment.

4. In cases of acute hematogenous osteomyelitis of the long bones with or without bacteremia, penicillin therapy will usually bring about rapid disappearance of evidence of disseminated sepsis, and usually there is a fairly prompt regression of the signs and symptoms of local inflammation at the site of localization.

The administration of penicillin to patients with chronically draining sinuses harboring staphylococci or streptococci will usually bring about a marked reduction in numbers or even disappearance of these organisms in the exudate, but direct culture of curettings from these sinuses may reveal persistent organisms not apparent on an ordinary swab culture. If no sequestrum is apparent roentgenographically the sinus may even become completely healed during the course of two or three weeks of treatment.

It was concluded that when penicillin, as administered systematically, it modified the course of most infections in which the causative organism was sensitive to penicillin in vitro.

Dramatic curative responses in disseminated sepsis were observed, particularly when the circulation to the localized distributing foci was adequate to effect a contact between the drug and the bacteria.

such cases surgical treatment which would have seemed unavoidable in the past, could be postponed or avoided altogether by the use of penicillin.

Favorable responses characterized by subsidence of toxemia, correction of anemia, rapid healing of infected or seriously contaminated wounds and elimination of infection within the pleural cavity or joints occur as well as failures. The latter occur particularly when the organism is insensitive or when the lesion under treatment is attributable only in part (or not at all) to the persistent activity of penicillin-sensitive bacteria, and under conditions in which penicillin cannot be brought to the infected area because of poor circulation or limited transport of the drug.

Careful bacteriological studies are essential if penicillin is to be used with maximal effectiveness.

STEPHEN A. ZIDMAN, M.D.

Bigger J. W.: Inactivation of Penicillin by Serum. *Lancet* Lond. 1944, 247-400.

Penicillin is inactivated by contact with human serum or blood. The degree of inactivation varies greatly with different specimens of serum and is much greater at body temperature than at lower temperatures.

This inactivation may lead to underestimation of the amount of penicillin in a patient's serum. Inactivation *in vivo* is probably important chiefly in cases in which the excretion of penicillin by the kidneys is slow.

JOHN J. MALONEY, M.D.

ANESTHESIA

Whalen E. J.: Anesthesia in Peroral Endoscopy. *Ann. Otol. Rhinol.* 1944, 53-469.

This article reviews anesthesia in peroral endoscopy. The endoscopic examination is not always possible under local anesthesia and general anesthetic methods are sometimes necessary.

It is suggested that all cases be individualized as to preanesthetic preparation and selection of type of anesthesia. The purposes of preanesthetic medication are elucidated and such drugs as pentobarbital sodium, morphine and scopolamine are discussed. In practice the ideal state of tranquility is effected by the use of morphine sulfate (gr. $\frac{1}{4}$) and scopolamine (gr. $\frac{1}{100}$). If these are given to an adult one hour before the administration of cocaine anesthesia for peroral endoscopy the patient will be quiet and co-operative and the amount of cocaine necessary to produce satisfactory anesthesia will be reduced to a minimum. When morphine and scopolamine are to be used a 1:25 ratio is maintained. The preanesthetic preparation of the patient with proper selection of the preliminary medication is of the utmost importance whether the basic anesthesia is of the local or general type.

Cocaine in 5 per cent strength has been found very satisfactory for the endoscopic procedures, the technique of using it is described in detail. The general inhalational anesthetic agents are discussed. Pen-

total has been found to be an anesthetic of high value when a general anesthetic is indicated. The disadvantages which are connected with its use can be anticipated and partly overcome. The administration of morphine and atropine one hour before the induction and the spraying of the pharynx and the larynx with cocaine hydrochloride (5 per cent solution) are methods used to prevent laryngospasm. Curare is a recent addition to the endoscopist's armamentarium, producing muscular relaxation in these cases of muscular spasm. Avertin is used infrequently because of its respiratory depression and the slow return of reflexes after its use.

Apomorphine (gr. $\frac{1}{40}$) is suggested as a counteractant of the ill effects of scopolamine overdose. Morphine has been discontinued in children and infants because of a few unfortunate experiences. The need for a clear airway is stressed. The respiratory depression which may occur during pentothal anesthesia must be treated by the establishment of a patent airway and inflation and aeration of the lungs.

Infants do not require anesthesia and preanesthetic medication for any endoscopic examination or operation. Children from three to fifteen years require general narcosis. This is best obtained with ether usually given by the open drip method. A small dose of atropine (gr. $\frac{1}{200}$ for the child of ten gr. $\frac{1}{300}$ for the child of five) is good premedication.

MARY KARP, M.D.

Buch I. M., Newton L., and Posner A. C.: Continuous Caudal Analgesia in Obstetrics. *Am. J. Surg.* 1944, 66-68.

One hundred and thirty cases of caudal-block anesthesia were reported by the authors in 50 cases single injections were made. The first 15 patients received 2 per cent procaine and the last 15 received 1.5 per cent metycaine. Continuous drip infusion was preferred because, once set up, it is automatic; it requires less unusual equipment than other methods and the obstetrician can visit the patient at his own convenience rather than at specific intervals as is required when other methods are used. A 19 G needle of $\frac{3}{4}$ inch length was used for the initial injection. After the test-dose period the needle was replaced by a 23 G needle through which a No. 5 ureteral catheter was threaded. The catheter was then hooked up to a graduated container connected by means of a Murphy drip chamber. The rate of flow usually required was about 12 drips a minute of 2 per cent procaine or 1.5 per cent metycaine.

Seventy-three of the patients were primiparas and 57 were multiparas. The amount of 2 per cent procaine required for a full initial effect was from 40 to 50 cc. and the amount of metycaine usually needed was from 30 to 35 cc. Two postpartum abdominal sterilizations proved refractory as to the height of the anesthesia. Caudal block has been discarded by the authors as being too unreliable for abdominal surgery because of the time factor and the occasional refractory cases.

The full effect of anesthesia from the initial dose was usually reached within fifteen or twenty minutes. The average duration of labor from the onset of the caudal block was three hours and fourteen minutes, the longest labor being eight and one-half hours.

Continuous caudal block had no effect on the duration intensity or frequency of uterine contractions but it had a relaxing effect on the cervix. After the discontinuation of the drip or after a single injection, analgesia lasted an average period of one hour and twenty four minutes.

Motor paralysis of the legs was more frequent among the patients who had had continuous caudal block of long duration. In only 1 instance was the drip discontinued because of a marked fall in blood pressure.

Complications were few: excitement and disorientation occurred in 9 cases, chills in 4, burning in 5, nausea and vomiting in 3, dizziness in 3, nonuterine pain in 10, uncontrollable desire to defecate in 1, and unilateral anesthesia of the perineum in 1.

The mechanism of caudal anesthesia was discussed. Absorption begins immediately and goes on continuously and its rate is never constant. A fair amount of procaine must be absorbed without entering into protoplasmic combination to produce anesthesia, and without even serving the usual function of maintaining that combination. If procaine is injected as soon as the caudal effect begins to wear off only a small amount is necessary to maintain the anesthetic level. If this level is allowed to fall, however, the amount of free procaine will fall considerably below the critical level in a large region, and considerably below the desired upper level. To regain the original level of anesthesia will now be a much more difficult problem.

The results in 97 cases were wholly successful. In 19 cases the block, though effective, was discontinued before delivery, and in 14 cases there was complete or partial failure or the dura was penetrated. Thirteen cases were refractory, that is the usual initial dose produced only a partial effect. In these cases small doses were injected at intervals until complete analgesia was obtained. Temporary motor paralysis of the lower extremities was noted in 13 cases.

Among the 49 patients in whom the blood pressure was carefully watched, 31 showed some depression. In 18 patients the systolic fall was at least 20 points. There were 3 fetal deaths in the series.

In conclusion, the author believes that confidence should be maintained in the method. In its present state, however, the inherent disadvantages obviate its universal use and thus preclude its acceptance as the long awaited panacea.

MARY KARP, M.D.

Williams, D., and Sweet, W. H. The Constitutional Factor in Anesthetic Convulsions. *Lancet*, Lond., 1944, 247, 430.

The purpose of this article is to report the results of electroencephalographic investigations of a series

of cases of anesthetic convulsions and to discuss the significance of the results obtained.

Of 42 patients with anesthetic convulsions, 40 had either the majority with nitrous oxide and oxygen, 11 had inductions with ethyl chloride, 1 had pentothal, and 1, divinyl ether. Electroencephalography was carried out on 22 of the patients, 13 of whom were males, 5 were children. Only 1 third had had acute inflammatory disorders requiring surgical intervention. The majority were "clean" cases and had a normal temperature at the time of operation. All anesthetics had been administered by experienced anesthetists and in every case the diagnosis of anesthetic convulsion was certain.

Abnormal electroencephalographic records were obtained from about three-fourths of these cases. Paroxysmal outbursts of abnormal cause were seen in more than half and larval epileptic headaches in a fourth of them.

The incidence and nature of the different abnormal discharges seen were identical with those found in idiopathic epileptics.

All the evidence presented supports the view that anesthetic convulsions are primarily due to a subnormal but latent epileptic liability. Factors which arise during anesthesia were mainly the precipitants of the convulsion.

MARY KARP, M.D.

Thompson, G. N., McGinnis, J. E., Van Harreld, A., Wierama, C. A. G., and Thet, E. R.: Electrocortical. Clinical Comparison with Electroshock. *War Med.*, Chic., 1944, 6, 53.

Electrocortical has been used as an anesthetic agent for animals. A clinical examination of the method in the treatment of schizophrenia was made in a study of 50 patients and the results were compared with those in a similar series of cases of patients treated by electroshock and by insulin. The conclusion was that electrocortical is superior to electroshock for schizophrenia, and is similar to insulin in its efficacy in the treatment of the disorder.

The standardized electrocortical technique is described in detail. A current of from 160 to 190 ma. was applied through electrodes bitemporally placed and was maintained for thirty seconds at the end of this time the currents were dropped to between 60 and 75 ma. At the end of from sixty to seventy five seconds, the current was raised at the rate of 5 ma. every fifteen seconds to a maximum of 125 ma. at five minutes. The treatment was usually terminated at seven minutes.

Certain neurological signs were seen constantly during the narcotic state produced by electrocortical. These were described and compared with electroshock.

In all three groups of patients studied, there was an initial cardiac arrest which usually lasted from three to seven seconds. In electroshock the tachycardia began shortly after the clonic phase, or about twenty seconds, and return to normal occurred usually within a few minutes. During the

entire duration of the current in the electroneurosis, the tachycardia continued and sometimes increased to rates of between 140 and 160 or sometimes even higher.

The principal difference was a prolongation of the stimulation of the autonomic nervous system but other phenomena not observed in electroshock were observed such as prolonged flexor tone and forced grasp. During deep insulin coma autonomic phenomena such as flexor tone and forced grasping were similarly present. The reactions of the patient during the postconvulsive phase of electroneurosis resembled those observed during insulin coma. It is believed that in its present status electroneurosis is not practical as an anesthetic device for human beings.

MARY KARP, M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Frantz, V. K., Clarke, H. T. and Lattes, R.: Hemostasis with Absorbable Gauze (Oxidized Cellulose). *Ann Surg* 1944, 120: 181.

A series of experiments were undertaken to reproduce as nearly as possible lacerated bleeding wounds such as those which in clinical practice might necessitate gauze packing. No adjuvant to promote clotting was used and no immediate effect was expected other than cessation of bleeding inherently due to the presence of the absorbable packing. These observations are based on experiments in which the wounds were made with the animals under general anesthesia, and with aseptic precautions.

The oxidized gauze was easier to pack into a bleeding wound than ordinary gauze. It seemed more pliable and when wet with blood slightly sticky. The oxidized gauze used dry was observed to swell when saturated, easily filling all the irregular crevices in the wound. The combination of blood and

oxidized gauze resulted almost immediately in a dark brown or black mass and as soon as this discoloration occurred bleeding usually ceased. The hemostatic effect appeared to depend not on clotting within the meshes of the gauze but on the swelling of the material and its sticky character when blood soaked so that the packing itself took the place of clot.

The authors have not studied any possible direct effect on the clotting process. Neutralization of the material with calcium acetate resulted in the loss of the described properties and rendered it less effective as a hemostatic. As early as twenty-four hours after packing the oxidized gauze was so friable that it broke when an attempt was made to withdraw it in contrast to ordinary gauze which could be withdrawn but which in clean wounds, especially was usually stuck, so that force was necessary for withdrawal. With ordinary gauze removal was apt to be followed by bleeding, which sometimes required secondary packing. With oxidized gauze in an open wound for forty-eight hours the gelatinous mass of brown material which represented the blood-soaked packing could be gently scraped away from the wound surface without renewal of the bleeding. Oxidized gauze even when not absorbed early was not invaded by reparative tissue. The foreign body therefore was not incorporated in scar to any extent and scarring was minimal. The absorbable gauze has also been used for hemostasis in 17 clinical cases.

This material even though soluble and relatively non-irritating is a foreign body in the tissues and remains as such often for several days. It should be used at least in wounds which are closed without drainage in as small quantity as possible. It is not a substitute for meticulous surgery and surgical principles must not be violated in its use.

LOUIS T. BYARS, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Rendich R. A. and Harrington L. A.: Roentgenologic Observations in Mesenteric Thrombosis. *Am J Roentg* 1944, 5 37

Although mesenteric thrombosis as a clinical entity has been recognized for over one hundred years very little attention has been given to the radiological diagnostic aspects of the disease.

The authors found one striking common finding in 3 cases. The KUB film of the abdomen revealed a distention of the intestinal loops and right half of the colon simulating a mechanical block. Gas collection ended abruptly at the splenic flexure. Gas distribution in the distended bowel corresponded to the distribution of the superior mesenteric vessels. The authors were somewhat surprised to find that no mechanical block existed when the patient was examined after he had been given a barium enema. This they have called a sign-complex that is the KUB film indicates mechanical intestinal obstruction whereas the barium enema reveals a colon filled with barium and no evidence of a block.

Three cases of mesenteric thrombosis are reported in which roentgenograms revealed distention of the intestines and right half of the colon corresponding to the superior mesenteric artery. It is the opinion of the authors that an early diagnosis aided by the roentgen findings offers an excellent opportunity for bowel resection and eventual recovery.

MAURICE D. SACIS, M.D.

Sahler O. D. and Hampton A. O.: The Roentgen Appearance of Common-Duct Stones. *Am J Roentg* 1944, 5 298.

Common-duct stones can often be demonstrated on plain abdominal roentgenograms or spot roentgenograms of the bile-duct area. They should be suspected in any case in which calcification is seen in the region of the gall bladder or common duct, in which calcium bile milk is demonstrated or in which the patient is jaundiced. The fact that common-duct stones can be seen on the plain roentgenogram is not generally appreciated. This is probably due to two factors: the relative infrequency of common-duct stones and the difficulty in demonstrating their location accurately.

Diagnosis of common-duct stones from the plain roentgenogram is dependent upon the presence of sufficient calcification to give a positive shadow. At the Massachusetts General Hospital, Boston, about 3 cases of easily demonstrable common-duct stones are seen per year at the present time.

The chief difficulty in the diagnosis of the common-duct stone without a contrast substance lies in establishing the correct location. The differentiation of common-duct stone from renal or cystic stone is the first problem to be solved. Since a stone in the cystic

duct may lead to hydrops of the gall bladder, while one in the common duct would not do so, the finding of a mass in the gall-bladder region associated with calculus is indicative of a cystic-duct stone. The cystic-duct stone may however not necessarily cause hydrops. If in the anteroposterior projection, a stone is seen to lie in the region of the duodenum or duodenal loop, the conclusion that it is in the common duct is justifiable since it will be below the juncture of the cystic and common ducts. In a rare case in which a dye study of the gall bladder has been made in addition to the plain roentgenogram, a diseased gall bladder may be found which retains its power of concentrating dye and subsequently contracts after a fatty meal. In such an instance, however, the bile duct would probably be outlined by dye and stones could still be accurately located.

HAROLD C. OGDEN, M.D.

Kenny M.: The Clinically Suspect Pelvis and Its Roentgenographic Investigation in 1000 Cases. *J Obst Gyn Brit Empire* 1944, 51 277

Roentgenographic examination was made in late pregnancy in 1,000 women. The objective of the survey was to determine whether or not roentgenograms could be of aid in those cases in which a previous history of abnormal labor or the clinical examination caused the physician to fear abnormal delivery.

The following types of conditions were investigated: (1) clinical pelvic contraction, (2) cephalopelvic disproportion, (3) fetal malpresentation, (4) clinical evidence of bone pathology, and (5) cases who had had a previous prolonged labor.

Before the beginning of the present work conflict, a combination of Thomas Caldwell-Moloy Roberts, and Rowden methods was used. As films became scarce and the diagnostic ability of the author improved a single anteroposterior film of the pelvis or even a lateral view would suffice. In all cases, an attempt was made to forecast labor. With increased experience the incidence of error in roentgenographic forecasts was low.

The Caldwell-Moloy classification of pelvis was used that is: gynecoid, android anthropoid or platycoeloid and platypelloid. Of the 1,000 cases examined, more than 900 belonged to the gynecoid, android or some combination of these types. 64 were anthropoid (platycoeloid), 18 platypelloid, and 6 pathological. A marked conformity was found between the physical form and the pelvic type. In 533 cases, the physical appearance and pelvic type conformed. 8.6 per cent (38 cases) anthropoid type, 7.8 per cent (118 cases) android type, 67.7 per cent (733 cases) gynecoid type. There were 106 cases in the anthropoid group and 43 in the gynecoid group.

A history was available in 540 of the 1,000 cases. Toxemias of pregnancy were in mild or severe form:

they occurred in 8 per cent of the gynecooid type, 10.9 per cent of the gynecoandroid, 78.5 per cent of the android, 57.7 per cent of the androgynecooid, 5.1 per cent of the anthropoid, and 12.7 per cent of the platypelloid. Puerperal morbidity was 23.9 per 1,000 cases and was higher in the android group.

As a result of the study the author believes that external antenatal measurements are negligible. There is no constant relationship between external and roentgenographic measurements. In pelviroentgenographic interpretation attention is given to the conformation of the sacrum and the posterior sagittal diameter of the midpelvis. During the six years in which this study was made, 10,197 women were delivered and roentgenographs were taken in 1,000 suspected cases. Of the 178 cesarean sections, 145 were done in the suspected group. Three hundred and seven of 342 forceps deliveries were done in the suspected group also. The gynecooid and android pelvis showed the lowest mortality rate. The author believes that routine pelvic roentgenographic measurements are essential, especially in the primigravida, and that undoubtedly they would help reduce untimely and ill-advised surgical procedures.

MAURICE D. SACHS, M.D.

Epstein B. S., and Davidoff L. M.: Iodized Oil Myelography of the Cervical Spine. *Am. J. Roentg.*, 1944, 52, 253.

The authors had the opportunity to study clinically and by means of iodized-oil myelography 5 cases of rupture of the nucleus pulposus of the lower cervical spine. There were 76 cases in the entire series of ruptured intervertebral discs, the remaining 71 occurring in the lower lumbar spine.

The myelography was performed by the lumbar route. With care it was possible to prevent entrance of the iodized oil into the cranial cavity, but when the oil did enter no difficulty was encountered in returning it to the spinal canal after the patient was placed in the upright position.

The detailed technique was as follows:

From 1.5 to 2 cc. of pantopaque or lipiodol were instilled into the lumbar subarachnoid space; then the patient was placed securely face down on a motor-driven tilt table equipped with a device for spot film roentgenography and the table was tilted according to the requirements of the fluoroscopic observations. As a rule it was necessary to invert the patient to an angle of from 70 to 85 degrees for the oil to enter the upper thoracic and lower cervical regions. If the oil passed too rapidly the table was returned promptly to the horizontal position until the proper rate of flow was obtained without entrance of the oil into the cisterna magna.

The myelographic appearance in the normal was established on the basis of a study of 8 patients who had myelographic examinations for other reasons than a lesion of the cervical spine and who had no symptoms or signs referable to the cervical region. It was noted that the opaque medium which had passed through the lumbar and lower dorsal spine as a solid

column had a tendency to break up into droplets of various sizes as soon as it entered the cephalad third of the dorsal spine. When this happened the patient was returned to the erect position to permit the oil to collect in the lumbar sac and the examination started anew. It was further observed that when the opaque medium finally entered the cervical spine as a solid column there always was a transitory delay of the passage of the column through the lower three cervical vertebrae. Following this pause, the column usually extended to either side of the canal, outlining the axillary pouches as tiny triangular shadows with their apices directed laterally along the cervical nerves as they pass through the intervertebral foramina. By tilting the patient up and down several times it was possible to collect most of the oil in the lower cervical canal.

The changes incident to herniation of the nucleus pulposus of the lower cervical spine were found to consist chiefly of alteration of the rate of flow and modification of the roentgen appearance of the solid opaque column. In 4 patients there was a definite partial obstruction to the passage of the column in the affected region which was fairly uniform and could be repeated in the same patient with identical results. In the fifth patient there was complete block of the cerebrospinal fluid. Serial spot roentgenograms made during the period of delay showed the opaque medium first gathered in a large globule with a flat or convex base simulating a capillary configuration; then a thin trickle of medium which passed from 2 to 5 cm. into one or both sides of the spinal canal, droplets being scattered beneath this and between the lateral ribbons. In the roentgenograms with the head downward there was a characteristic inverted U or L appearance. In contrast with the normal the oil did not enter the axillary pouches. When the obstruction was complete the roentgen picture could not be distinguished from that observed in extramedullary tumors.

The 5 cases are described in short résumés. Several roentgenograms are reproduced for the purpose of illustration.

The general conclusion is reached that whereas routine roentgenographic and clinical examinations may lead to confusing results in the diagnosis of herniation of the nucleus pulposus of the lower cervical spine, myelography of the cervical canal constitutes a procedure which can provide valuable information and which, therefore, merits further careful study.

T. LEUCUTIA, M.D.

Long, L.: The Noninjection Method for Roentgenographic Visualization of the Internal Semilunar Cartilage. *Am. J. Roentg.* 1944, 52, 269.

The correct diagnosis of injuries to the knee cartilage is of special importance in military medicine where such a diagnosis eliminates a man from combat duty and usually from the service. Routine roentgenography of the knee is rarely helpful except in ruling out bone lesions and certain loose bodies.

There has been considerable literature concerning the roentgen demonstration of the semilunar cartilages by means of injections of the knee joint with gas or radiopaque solutions, but in military medicine these are considered operative procedures which may alter the line of duty on account of subsequent developments and therefore would not ordinarily be used as routine.

The author employs the noninjection method outlined by Reynolds in 1941 and in this article he publishes the results of a series of 709 examinations. The method is so simple that it is within the capabilities of a good technician.

The principle of the method is that an anteroposterior roentgenogram is made about three seconds after the end of a maneuver consisting of strong traction firm internal rotation and abduction of the fully extended leg. The thigh is held tightly against the table by a strong immobilization band with a fixed padded fulcrum against its lateral aspect just above the knee. To facilitate the easy adaptation of this fulcrum to either side of the table, the author constructed an accessory which he describes as follows. It consists of a piece of 3/4 inch plywood about 3 feet long and of width sufficient to fit inside of the metal rails at the sides of the table top. If there are no rails on the table, a flange will have to be added to each side of the board to prevent sideplay. In the center running lengthwise, is a 5 by 16 inch opening, and midway on one side of this is a padded fulcrum securely attached to the board. By simply turning the board end-for-end it may be used for either right or left knee.

The results of the examination are arranged in Table I.

The 15 cases of Group VII in which operation followed the roentgen study are arranged in another table according to the roentgen findings, operative findings and the pathological report. In 13 of these (86.7 per cent) no cartilage shadow was present in the roentgenograms. Two revealed distinct cartilage shadows with a defect conforming to the air replacement shadow.

In 13 patients one or both knees were examined two or more times with a total of 125 examinations in addition to the first one. The results of the re-

examinations are given in a third table. Surprisingly in a rather considerable number of cases in which the initial examination failed, the re-examination was successful. This is blamed partly on the lack of experience of the technician and partly on the failure of the patients to completely relax during the first examination. In any event, it is advisable to make a second or third examination whenever the cartilage does not appear to be definitely outlined at the initial examination.

The author presents some beautiful roentgenograms for the illustration of normal and various pathological semilunar cartilages. The negative shadow which appears as a result of the maneuver around the cartilage and which makes its visualization possible is the result of partial vacuum rather than of air.

The following general conclusions were arrived at by the author following this very minute and detailed study:

1. The technique of Reynolds for the localization of the internal semilunar cartilage requires careful attention to small details for success and should not be attempted after a recent injury.

2. In normal asymptomatic knees, the cartilage was visualized in 67.2 per cent of the cases in the first attempt. Re-examination increased this percent age to 75.4 per cent.

3. In pathological conditions (mostly without surgical confirmation) the cartilage could be visualized in only 10.8 per cent of the cases, which indicates that nonvisualization is a corroborative sign. When an abnormal cartilage became visible, often a defect, thinning, or absence of its wedged shape as noted. Reynolds states that the cartilage cannot be demonstrated in the presence of effusion regardless of whether or not it is injured, and this was also the author's experience. Acute tenderness was likewise found to be a contraindication to the use of the method.

4. Improvement in accuracy of interpretation may be expected when a large series of surgically treated cases can be analyzed. For the present, it is best to interpret the roentgen findings in the light of the available clinical evidence.

T. LAURITZ, M.D.

TABLE I—RESULTS OF EXAMINATIONS

	Cartilage demonstrated	Cartilage not demonstrated	Total
Group I Normal, asymptomatic knees	104 (87.0%)	15 (13.0%)	119
Group II Symptomatic knees with final diagnosis other than pathological cartilage	75 (66.4%)	38 (33.6%)	113
Group III Clinical diagnosis of pathological cartilage without surgical follow up	1* (17.0%)	5 (83.0%)	6
Group IV Probable pathological cartilage but no definite diagnosis made		41 (100%)	41
Group V Symptomatic knees with records not available for classification	18 (41.0%)	26 (59.0%)	44
Group VI Previous knee operation elsewhere but no record as to the exact procedure		1 (100%)	1
Group VII Pathological cartilage with operative confirmation	2* (3.3%)	5 (86.7%)	7

*Eight of them showed defect or thinning of the lateral portion.

**Both with defect.

Ungar E. M. Spiegler G. and Smithers, D. W.:
The Volume Localization of Deep-Seated Tumors by Means of Tomography *Brit J Radiol*
1944 17 235

In recent years more attention has been given to tumor dosages in roentgen therapy. The trend at present is not to consider the dosage at a given point within the neoplasm but to consider the tumor itself as a three-dimensional object with the rays entering into it from many fields.

The authors are concerned with reconstruction of the tumor in volume in its correct relationship to the body. It was found that tomography could be used for such a purpose. A description of the principle of tomography (sectional roentgenography) is given. An estimate was made concerning the magnification at each plane and a correction table established. In this manner with multiple films at varying levels throughout the tumor a model of the entire tumor could be reconstructed in its relationship to the body.

Tomography is a diagnostic field and it is the responsibility of the diagnostic roentgenologist to render accurate interpretation of the tomograph and to co-operate with the therapist in an effort to administer the correct estimated tumor dose. However, it is pointed out that tomography is an adjunct to routine films and does not supplant them.

MAURICE D. SACHS, M.D.

Veloso M. M. Bronchial Cancer Treated with X rays (Cancer bronchial tratado con rayos X). *Rev méd. Chile* 1944 72 616

A case of bronchial cancer in which the patient is alive and free of recurrence five years after treatment is discussed. On admission to the hospital in November 1938 the patient was forty-six years of age and weighed 60 kgm. he was in good general health and had no past history except mild attacks of bronchitis in winter. He came for examination on account of a sudden intense pain in the left half of the thorax, cough without expectoration, dyspnea, and a temperature of 38°C. Clinical examination showed a pleural friction rub at the left base and relative dullness in the same region. Roentgen examination showed slight paralysis of the left diaphragm and veiling of the left costodiaphragmatic sinus. A diagnosis of pleurisy probably tuberculous, was made and the patient sent to a tuberculosis sanitarium. Examinations for tuberculosis were negative however and he was discharged.

Ten weeks later he returned on account of pain in the precordial region and left half of the thorax, with cough, copious expectoration, sweating and chills and a temperature of 38°C. He had lost seven kgm. in weight since the last examination. There was relative dullness of the left hilar region, with a murmur indicating a cavity, medium and low rales were heard. Roentgen examination showed a cavity containing liquid. The patient was hospitalized with a diagnosis of acute lung abscess, for which he was treated with small doses of neosalvarsan

and intravenous injections of 20 per cent alcohol in glucose solution and 4 per cent emetin. His condition showed improvement but in order to confirm the decrease in the size of the abscess planigrams were taken. These planigrams in addition to showing the disappearance of the cavity, showed decreased transparency of the left upper lung field and a slight constriction of the bronchus on that side. This suggested compression of the bronchus with atelectasis due to bronchial cancer. Roentgenograms with lipiodol showed obstruction of the left bronchus and bronchoscopy showed a congested tumor which had the appearance of bronchial cancer. Histological examination of a biopsy specimen showed an anaplastic adenocarcinoma, evidently embryonic with intense karyokinetic activity and therefore, sensitive to irradiation.

Beginning July 18, 1939 a total dose of 7,500 international roentgen units was given in about three weeks the factors were as follows: individual doses from 400 to 500 roentgen units, 200 kv., 90 cm. focus-skin distance and 300 sq. cm. of irradiated surface. With a filter of 1 mm. of copper and 0.8 mm. of aluminum this gave a dose of about 2,300 international roentgens to the tumor.

The patient was dismissed without fever or pain and weighing 54.1 kgm. There was scanty expectoration. Roentgenograms have been taken at intervals since then. The roentgenograms taken before and at various periods after treatment are given. The patient is in good condition.

AUDREY G. MORGAN, M.D.

MISCELLANEOUS

Hempelmann L. A., Jr., Reinhard E. H., Moore C. V., Bierbaum, O. S., and Moore, S.: Hematologic Complications of Therapy with Radioactive Phosphorus. *J Lab Clin Med* 1944 29 1030

One hundred sixteen patients with various types of hematologic dyscrasias have been treated with radioactive phosphorus at the Washington University School of Medicine, St. Louis, Missouri and 100 of these have been observed for a sufficiently long period of time to permit evaluation of the therapy. Radioactive phosphorus is a valuable therapeutic agent in the management of polycythemia vera and the chronic forms of leukemia. Its use in patients with most acute leucemias, Hodgkin's disease, reticulum-cell sarcoma and lymphosarcoma has been disappointing. The primary purpose of this communication is to call attention to the frequency with which anemia, leucopenia, and thrombocytopenia developed in the patients treated.

The appearance of toxic effects induced in the peripheral blood by radioactive phosphorus may be delayed for many weeks, presumably because with its half life of fourteen and three tenths days it continuously emits radiant energy for many weeks.

The authors used a freshly prepared solution the initial activity of which usually varied between 300

and 400 microcuries per cubic centimeter. The solution was used during a period of weeks until its strength had decayed to between 50 and 50 microcuries per cubic centimeter. Small frequent intravenous injections of radioactive phosphorus were used. The size of each dose given parenterally varied between 100 and 2,000 microcuries. Patients were usually treated two or three times a week at first. As the white-blood-cell count either approached normal in the patients with leukemia or became subnormal in the cases without initial elevation of the leucocyte count, the dosage was decreased and the time interval between treatments was lengthened. Patients with polycythemia were given larger quantities of radioactive phosphorus at much less frequent intervals. Therapy was governed principally by the changes in the peripheral blood, and an attempt was made in each case to restore the cytology of the blood to as near normal as possible and to maintain this effect.

In the cases of lymphosarcoma, Hodgkin's disease, reticulum-cell sarcoma, multiple myeloma, and giant follicular lymphoblastoma, in which the white-blood-cell count was not elevated, regulation of therapy was more difficult. Administration of radioactive phosphorus was continued in these instances until changes in the peripheral blood gave warning of a depression of bone-marrow activity. In some patients serial bone marrow aspirations were made to aid in regulating therapy. Patients with subleukemic leukemia were given amounts that were comparable with those required to regulate the subjects with elevated counts.

The most striking complication was the thrombocytopenia. The platelet count fell to below 100,000 per cubic millimeter in 44 instances and to below 50,000 in 33 of these. The fall in platelets frequently developed in patients with leukemia, for instance, several weeks or months after the leucocyte count had approached normal and most of the abnormal cells had disappeared from the circulating blood. In

some cases, thrombocytopenia occurred even after therapy had been discontinued. Of the 44 patients who developed thrombocytopenia, 38 showed clinical manifestations of abnormal bleeding.

In 56 patients there was a steady progressive decrease in the leucocyte count; in 25 the white blood-cell level first increased and then showed a progressive decrease. In 2 patients with acute leukemia there was a gradual rise in the number of leucocytes up to the time of death. Three patients who were in the terminal stages of leukemia first showed a decrease followed by a progressive increase. In the 14 others there was either no significant change in the leucocyte count or a pre-existing trend was apparently uninfluenced by therapy. Of the 41 patients who developed leucopenia apparently as the result of therapy, 6 had definite ulceration of the mouth or nasopharynx, the 35 others had no specific symptoms which could be attributed directly to the leucopenia.

Thirty-six of the 100 patients developed an anemia which seemed to be due to the therapy; this included only patients whose erythrocyte count dropped by 1,000,000 or more cells per cubic millimeter and to a level below 3,500,000.

At autopsy localized areas of necrosis in the bone marrow were observed several times. In 4 instances, the bone marrow was found to be aplastic.

There was considerable variation in the susceptibility of different subjects to the toxic effects of radioactive phosphorus. In several instances, leucopenia, thrombocytopenia, or an anemia followed comparatively small doses of the material. Much larger amounts were tolerated by other patients without difficulty. The dosage must be individualized to a high degree. The blood of patients treated in this manner should be studied at frequent intervals so that the hematologic changes can be recognized early and further administration stopped before irreversible toxic effects on the bone marrow are produced.

HAROLD C. OCHSNER, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Romano, J. Engel G. L. Ferria, E. B. Jr. Ryder H. W., and Others. Problems of Fatigue as Illustrated by Experiences in the Decompression Chamber. *War Med. Chic.* 1944, 6: 102.

Fatigue studies on 43 adult subjects, repeatedly exposed to simulated altitudes of 35,000 feet in a decompression chamber were carried out with clinical, psychological, and laboratory tests. Physical and chemical studies have been of little value in the understanding of fatigue in persons who are not subjected to severe muscular effort, or who are not deprived of adequate sleep. The problem of fatigue in flyers does not depend totally on physical stresses.

This study considers stresses other than muscular effort which contribute to fatigue such as anxiety and individual emotional flexibility. Eight subjects were studied intensively, psychologically, and physiologically before and after the six month period of exposures. In addition to detailed personality analysis, attention was directed to the previous individual patterns of fatigue as related to different types of stress. Electroencephalographic studies were also made under varying conditions.

Three types of fatigue were observed. Muscular fatigue was most pronounced in the first or second flight and occurred in almost all subjects. It disappeared with training and was not related to decompression sickness. A second type of fatigue was related to boredom or ennui. This also tended to occur during flights without decompression sickness when the subjects remained inactive at altitude for long periods, and disappeared quickly after descent. The third type of fatigue was not related to either muscular work or boredom. It began sometimes immediately but more often a few hours after descent, and tended to diminish in frequency and intensity with experience. It was experienced by 24 of the 43 subjects. The character of this fatigue was similar to that previously experienced in anxiety stress situations and showed no direct correlation with decompression sickness in many instances. Physiological derangements could not be demonstrated quantitatively and objective evidence of such disturbances could be found in only a few instances after severe decompression sickness. Laboratory data, including the electroencephalogram, blood count, and circulatory reactions to changes in posture, revealed no direct correlation in any type of fatigue. While certain subjects experienced more pronounced fatigue after severe decompression sickness, others did not.

These data do not support the concept that subclinical bends accounts entirely for this type of fatigue. On the other hand it is likely that the diffuse tissue damage which undoubtedly occurs in

decompression sickness will as in other types of tissue damage lead to fatigue or augment and prolong the fatigue of emotional stress. The findings suggest that emotional factors play an important role in the production of the third type of fatigue. The importance of a more thorough understanding of the person who experiences fatigue is emphasized.

JOHN L. LINDBQUIST, M.D.

Ficarra, B. J., and Naclerio, E. A. The Physiochemical Disturbance in a Severe Burn. *Sur.* 1944, 16: 529.

The most neglected phase of the burn problem has been the physiochemical disturbance produced by tissue destruction. The changes reflected in the circulating blood due to severe burns in a human being have been studied rarely. Most of the data have been gathered from animal experimentation. In the treatment of burns the opportunity and facilities were available on one occasion for a detailed and continual physiochemical observation of a severely burned patient. In view of the fact that few complete chemical analyses have been made in clinical burns the following case report was considered significantly valuable.

A forty-three year-old white male was burned when his clothing became inflamed from sparks which arose from the wire he was repairing. Tannic acid was applied to the body surface by members of the fire department and he was then taken to the hospital. The patient was in shock from burns involving 60 per cent of his body surface. There were third-degree burns of both thighs, second- and third-degree burns of the right arm and forearm, and first and second-degree burns about both ankles. In addition he had a fracture of the left ankle. At this time his temperature was 99.6 F, pulse 120, respirations 26, and blood pressure, 90/50.

Nine hours after admission the patient had responded sufficiently from shock to permit treatment of the burn. One hundred cubic centimeters of whole blood were taken for study immediately after entrance. For the first sixteen hours blood-chemistry studies were done every four hours. Thereafter complete studies were made every day. On the seventh postburn day the only available vessel for obtaining a blood sample was the internal jugular vein. This was due to the fact that the burn areas prevented the use of many vessels; others became thrombosed and on that day the patient became edematous. On the ninth postentrance day the patient's temperature rose to 102 F and he became delirious. Two days prior to this a toxic erythematous rash became visible on the nonburned skin surfaces. The patient expired on the tenth hospital day in spite of the general therapy with whole blood, plasma fluids, adrenocortical extract, vitamins, chemotherapy, protein, and local treatment of the burn areas.

The anatomical findings at autopsy were as follows: primary diffuse third-degree burns of the head, chest, back and upper and lower extremities; pyoderma with ulceration; bilateral acute and chronic interstitial pyelonephritis and nephrosis; bilateral adrenal hemorrhage; passive congestion of the liver; hemorrhagic exudate; acute tracheitis; ulcerative vaginitis; mucosal hemorrhage throughout the gastrointestinal tract; cardiac hypertrophy with right ventricular dilatation; pulmonary edema and bronchobronchitis with calculi.

The significant pathological findings were revealed in the study of the kidneys, liver and adrenal gland. Among these four organs the most interesting findings were noticed in the kidneys.

Usually the kidneys were extremely large; the right one weighed 40 gm. and the left 350 gm. The capsule was thin and stripped easily. The underlying cortical surface was reddish brown in color with readily demarcated cortex and medulla. The glomeruli were grossly prominent. Microscopic examination of the kidneys demonstrated that the glomerular spaces were distended with albuminous deposit. The cytoplasm of the tubular epithelium had a ground glass appearance, especially in the proximal convoluted tubules. Many tubules contained albuminous material. A marked interstitial edema with scattered localized areas of hemorrhage was present. The renal pelvis, medulla and subcapsular region showed dense collections of lymphocytes, plasma cells and fibroblasts. The capillaries showed pronounced dilatation and engorgement.

Pathological histology of the liver showed a generalized dilatation and engorgement of the sinusoids. The liver cells indicated passive congestion. Lymphocytic nests with occasional polymorphonuclears were seen about the portal region.

The adrenal glands retained their normal histology. However, the zona reticularis of the medulla contained hemorrhagic areas. The cells had a coarse ground glass appearance. Marked interstitial edema was seen in all the zones of the medulla.

It has been generally accepted that the extensive burns are toxic, the results because of injurious elements produced by burned tissues. The quantity of liberated toxic substance which passes into the circulation is believed to be proportional to the extent of the burn. The exact nature of this toxic substance has never been determined. Formerly it was thought to be derived from the albumin of the cell and was expected to be a polypeptide. Death was attributed to the physiological pathological alterations in the internal organs due to this proteolytic substance.

From their experience with burns the authors believe that the question cannot be answered simply by stating that toxic is the cause of physiological dysfunction. If relatively minimal consideration has been given to the physicochemical changes in burns. In 1924 Davison studied intensively the sodium-chloride metabolism in burns. This was the first time that an evaluation of the blood chemistry found a prominent place in the lives of burns. He

found a significant lowering of the chlorides, it was believed to be due to a lowering of the chloride levels below the renal threshold rather than to a primary kidney change. It was further assumed that the chlorides did not fall immediately after the burn but diminished progressively during the first few days.

Fox in a recent publication, has stressed the importance of sodium in the rational treatment of the burned patient. Hypoproteinemia, contractility of body protoplasm in alterations in carbohydrate metabolism, hemoconcentration and acidosis have been noted and discussed by many observers.

The major concern in the treatment of burns is the administration of intravenous fluids that restore the blood volume and its physicochemical components to nearly normal levels. The perfect plasma is based upon the fact that extensive burns are followed by exsiccation and cellular concentration of the blood. Harkins devised a simple method of calculating plasma dosage. His formula is to give 1 cc. of plasma for every point the hematocrit is below the normal of 45.

The authors have emphasized that the intelligent management of the severely burned patient demands daily biochemical diagnosis. The facility with which an altered physicochemical state occurs merits constant checking of the blood chemistry. Therefore it can be stated that blood chemistry determination is equally as important as the diagnosis and the definitive treatment of the severely burned.

The authors found that the analysis of the metabolic and chemical data in this fatal burn case indicated sodium chloride changes by gross destruction of body protoplasm in all ratios in the electrolyte metabolism and hemoconcentration.

The acidosis which usually accompanies the burn syndrome was absent. An unexpected alkalosis occurred following the administration of citrate sodium on the fifth postburn day.

Emphasis is placed upon a study of the blood chemistry on or about the fifth day. At this time a break in the biochemical harmony occurs. This condition is manifested by an elevation of the effects of nitrogen metabolism associated with a serum protein, plasma sodium, and blood calcium.

In the treatment of this patient 10,000 cc. of fluid were administered parenterally. Of this amount 6,000 cc. were plasma and 3,100 cc. were blood.

Death on the tenth day was attributed to exhaustion and renal failure. The major factor indicating the cause of death in burns has not been established satisfactorily. It is believed that a severely burned patient dies of physical exhaustion and therefore a study of the organs involved in the process of physiology (liver, kidneys and adrenal) is essential in the determination of the problem of the ultimate lethal factor.

Herein lies the intrinsic value of blood studies of the physicochemical changes in the burned.

reflected in altered blood chemistry. The exhaustion of the aforementioned basic physiologic organs may be the cause of death when after the second week the patient seems to be improving.

This somatic distress is emphasized because during the third week the initial danger apparently has been overcome. The anxious surgeon considers the patient sufficiently improved for a skin graft. However, the disturbed chemistry has not been restored. In the presence of this metabolic discord, the administration of an anesthetic plus the surgical procedure may be sufficient to cause death.

BENJAMIN GOLDMAN M.D.

Taylor F. H. L., Levenson, D. M., and Adams, M. A. Abnormal Carbohydrate Metabolism in Human Thermal Burns. *V. England J. M.* 1944, 331-337.

In a study of 35 consecutive burned patients a high incidence of hyperglycemia, lactic acidemia and a moderate reduction in the carbon dioxide-combining power of the plasma were found. There is a high degree of correlation between these abnormalities of carbohydrate metabolism and the severity of the burn. The glucose tolerance tests made indicate that in some severely burned patients with hyperglycemia there remains a considerable ability to metabolize added glucose.

There was no evidence of liver damage in these patients as a result of the burn. In the few cases in which liver damage was found it was present before the injury being for the most part an alcoholic cirrhosis.

The abnormalities in carbohydrate metabolism presented are not inconsistent with the presence of an increased glycogenolysis together with a possible gluconeogenesis from protein. It is suggested that additional glucose be given early to burned patients.

SAMUEL KAIM M.D.

Jones, G. M.: Diabetes Insipidus; Clinical Observations in 42 Cases. *Arch. Int. M.* 1944, 74-81.

Diabetes insipidus is a syndrome produced by damage to the supraopticohypophyseal tract and is not a specific etiological entity. This fact is too little recognized by the medical profession in general. A historical summary of the experimental and clinical contributions which lead to the present knowledge and concepts of diabetes insipidus is presented, and an analysis of 42 cases is made. The causes of the diabetes insipidus in these cases are listed in Table I.

One of the striking features of the cases studied was the early age of onset of the diabetes insipidus. Any patient with symptoms of diabetes insipidus deserves the most careful study in an attempt to determine the specific pathological changes that are responsible for the symptoms. The term "idiopathic diabetes insipidus" merely indicates that the pathological cause was undetermined before death or that the polydipsia and polyuria had a possible psychic origin. The latter possibility can be eliminated by a

TABLE I—CAUSES OF DIABETES INSIPIDUS

	No. of cases	Percentage
Tumor of pituitary gland	11	26
Tumor of hypothalamus	3	5
Hand-Schüller-Christian disease	4	10
Chronic encephalitis	7	16.6
Syphilis	3	7
Post-traumatic injury to the head	3	7
Pituitary infarction (?)	1	2.4
Cerebrovascular accident	1	2.4
Subarachnoid hemorrhage	1	2.4
Hypothalamic damage, cause unknown	1	2.4
Undetermined cause	8	19
Total	43	100

prolonged urine-concentration test since the polyuria is primary and the polydipsia secondary, and the patient with true diabetes insipidus will continue to have a large volume of urine of low specific gravity with resultant dehydration and loss of weight during such a test. In any case in which such a response is obtained the diagnosis of organic damage along the supraopticohypophyseal tract should be made. Furthermore, since diabetes insipidus is not infrequently the first symptom in cases of neoplasm (occurring as early as six years before other evidence of the malignant growth in one of the cases reported here) roentgen irradiation of the hypothalamohypophyseal region may be worth while when the cause of the diabetes is undetermined. Roentgen irradiation is also of value in Hand-Schüller-Christian disease. For patients with diabetes insipidus who do not respond to therapy as specifically indicated by the etiological factor, substitution of the antidiuretic principle in the form of a solution of extract of the posterior lobe of the pituitary gland or pitressin affords notable symptomatic relief. Of the various methods of administration of this extract as replacement therapy in the absence of the antidiuretic principle the intramuscular injection of pitressin tannate in oil seems the most desirable. The intranasal application of pitressin in jelly was the least satisfactory of the methods tried in this series. The use of a low salt as an adjunct to other therapy may be of benefit in any case of diabetes insipidus. Thyroidectomy should not be performed for diabetes insipidus unless there are other specific indications for the procedure.

JOHN L. LINDBQUIST M.D.

Free, A. H. and Leonards, J. R.: Studies on the Ingestion of Large Quantities of Protein and Amino Acids. *J. Lab. Clin. M.* 1944, 29-963.

Studies are reported in 3 normal human subjects in whom comparable massive amounts of whole blood protein, muscle meat, and amino-acid mixture were ingested over an eight hour period. Studies of the blood urea, blood amino acids, urinary urea excretion, and urea clearances were carried out.

The limiting factor in determining the amount of protein or amino-acid mixture that can be ingested appears to be the rate of intestinal absorption. Large amounts of unhydrolyzed protein are more

rapidly handled by the normal gastrointestinal tract than are equivalent amounts of amino acids. It seems questionable therefore whether amino acids have any advantage in alimentation over unhydrolyzed dietary protein especially when large amounts are administered and when pancreatic proteolases are present in adequate amounts. After the ingestion of the two proteins and the amino-acid mixture the variations in the blood levels of urea nitrogen and amino-acid nitrogen were similar.

Maximum urea clearances as well as urinary urea excretion were increased after the consumption of amino acids and proteins. The extent of gastrointestinal hemorrhage can be more accurately evaluated by urine and blood-urea determinations than by blood studies alone. WALTER H. NADLER, M.D.

Wallace, D. H. and Adler Tana, P.: A Study of Vitamin C Saturation in Hospital Children. *Glasgow M J* 1944, 42: 55

Vitamin C saturation tests performed on 838 children admitted to the wards of the Royal Hospital for Sick Children during the period from October 1940 to June 1944, showed defective vitamin C nutrition in a high proportion of the children. This was most severe in the year from October 1941 to September 1942, when because of war conditions vitamin C in the diet was at its lowest.

Since febrile illnesses reduce vitamin C reserves precautions should be taken in the medical wards of children's hospitals to ensure that ample vitamin C in one form or another is given to all the patients.

The children most of whom came from the slum districts of Glasgow showed subnormal vitamin C saturation when compared with children living under good conditions. The deficiency was especially noticeable in the year when the dietary sources of the vitamin were at their lowest. It is thought that the low vitamin C saturation found in the children admitted to the hospital was partly due to the fact that many of them were suffering or recovering from various acute infections such as pneumonia or gastroenteritis.

The influence of infection in lowering the vitamin C reserves was evidenced by comparison with patients from the same social class who were admitted to the surgical wards of the hospital but who were suffering from noninfective conditions.

Frank scurvy was rare, and this suggests that optimal saturation is not necessary for average health. When repeated test doses of the vitamin were given, a high proportion of the children who were unsaturated when first tested showed suboptimal saturation within three days. Most of those who took longer to become saturated were suffering either from scurvy infection or some nutritional disorder in which there is interference with absorption from the bowel. While full saturation may not be necessary for the maintenance of health, it appears that children living in slums, where acute infections are so prevalent, should have ample supplies of vitamin C because with the onset of infection their reserves become exhausted. STEPHEN A. ZITMAN, M.D.

Powers, J. H.: The Abuse of Rest as a Therapeutic Measure in Surgery. *J Am M Ass* 1944, 113: 1079.

The author notes that rest, as a therapeutic measure is fraught with hazard. Prolonged periods of recumbency in bed are anatomically physiologically, and psychologically unsound and unscientific. Surgical wounds heal firmly even though early postoperative activity is encouraged. Infants and young children cannot be kept quietly at rest in bed after operation yet postoperative hernias are not common.

The author presents 100 consecutive patients who were allowed to sit in a chair and to walk on the first day after major operations and compares these studies with similar observations on an equal number of conservative, unselected patients who remained in bed for the traditional period of from ten to fifteen days.

The operations performed were as follows: hernioplasty for inguinal, femoral, umbilical, epigastric, and incisional hernias; appendectomy for acute appendicitis including cases of perforation with abscess and peritonitis; cholecystectomy with and without exploration and drainage of the common duct and hysterectomy and other major pelvic operations performed through an abdominal incision. The patients in both groups were all over twelve years of age.

Of the patients who underwent hernioplasty 39 were up and walking on the first day after operation and an equal number remained in bed from twelve to fourteen days. Those who were permitted early activity spent an average of nine and one-tenth days in the hospital and required five and six-tenths beds for convalescence while the other group remained in the hospital fifteen and two-tenths days and did not return to work until ten weeks after operation. No recurrences developed among those who were up on the first postoperative day while 1 inguinal and 1 femoral hernia recurred among the recumbent patients.

Of the patients with acute appendicitis, 23 from each group were observed. Those who were activated promptly returned to work in four and eight-tenths weeks, while those who remained in bed the customary time did not resume their work until eight and seven-tenths weeks after operation. There were no postoperative residual intraperitoneal abscesses that developed in the patients who were ambulatory early in the other group, 2 such abscesses developed.

Of the patients who underwent cholecystectomy 14 from each group were observed. One in the ambulatory group developed a late incisional hernia subsequent to discharge from the hospital, while 2 such hernias occurred in the patients who remained in bed sixteen and twenty days after operation, respectively. The convalescence in the hospital was materially shortened and the total average period of rehabilitation was reduced one half by early postoperative activity.

Twenty five patients of each group were observed after abdominopelvic surgery. Supravaginal hysterectomy was performed 10 times in the ambulatory group while it was performed only 8 times in the other group. Only 1 person was allowed up on the first day after repair of a cystocele, rectocele, and prolapse. The average age of the patients in the early and control series was almost exactly the same. The length of time spent in the hospital after operation and the total period of convalescence for the patients who were allowed early activity were eleven and seven-tenths days and six and seven tenths weeks, respectively for those whose regimen followed the earlier pattern; the averages were sixteen and seven-tenths days and eleven and six tenths weeks respectively.

Of 100 patients observed in each group the ambulatory patients spent ten and three-tenths days in the hospital while those who followed the traditional convalescent program averaged sixteen and one-tenth days in the hospital. This represents a saving of 580 hospital bed days. If the temperature and pulse rate are regarded as accurate indexes of convalescence such early activity is in no way deleterious. However other complications may arise.

Postoperative complications may be classified as local pulmonary, cardiac, vascular, genitourinary, gastrointestinal, and general. No local complications of major significance occurred because of early activity. No wounds disrupted. One incisional hernia developed several months after operation, an incidence of 1 per cent. Two incisional hernias, 2 recurrent hernias, 1 hematoma, and 1 silk sinus occurred among the patients who were kept recumbent for the customary postoperative periods. Serious pulmonary complications were likewise more common among the patients who remained in bed. No cardiac complications were observed among the ambulatory patients. The incidence of vascular complications was reduced but not eliminated. Postoperative inhibition of the bladder was rather common in both groups. Repeated catheterizations were much more frequent among the patients whose convalescence was spent in bed. Postoperative dilatation of the stomach and fecal impactions occurred only in the patients who remained in bed. Fever which could not be explained by reaction to operation or to the disease was observed in 5 patients among the recumbent group. In total there were 17 postoperative complications among the 100 patients who were out of bed on the first day and 46 among the same number in the unselected control group.

Accurate reapproximation of the tissues is compulsory if early activity is planned. Nonabsorbable, interrupted sutures are preferred except in the peritoneum which may be closed with a continuous stitch. Additional supporting sutures of silk worm gut or silver wire may be desirable for obese patients or in the presence of infection.

In conclusion the author notes that early postoperative walking may reasonably be of definite

therapeutic value in the prevention of pulmonary complications. Elevation of the diaphragm in the recumbent position, pooling of the tracheobronchial secretions in the finer ramifications of the bronchial tree, the patient's disinclination to cough because of pain, the limitation of maximal respiratory excursions and the invariable reduction in the vital capacity after laparotomy or hernioplasty all play some role in the etiology of postoperative atelectasis and pneumonia. The volume of the tidal air, tension of the oxygen in the alveolar spaces, oxygen saturation of the arterial blood, and the depth and rate of respiratory movements are increased by exercise.

The occurrence of 1 case of iliofemoral thrombophlebitis and 1 of suspected thrombosis in the deep veins of the leg among the ambulatory patients indicates that early postoperative walking does not entirely circumvent the formation of thrombi. It may obviate the liberation of emboli of sufficient size to precipitate a fatal postoperative catastrophe. A thrombus of this magnitude does not usually develop in an active venous circulation.

Postoperative dysfunction of the gastrointestinal tract is uncommon when early convalescent activity is permitted. Abdominal distention is rare. Enemas, rectal tubes, and poultices are seldom necessary. A regular diet can usually be accepted on the fourth or fifth postoperative day.

The absence of asthenia in ambulatory patients is impressive demineralization of the bones and atrophy of the muscles, so common after prolonged periods of rest in bed are entirely obviated.

Contrary to the opinion of the majority of surgeons, those who have advocated early postoperative walking have observed no deleterious effect as a result thereof, no increase in pain, and no greater frequency of disruption or hernia.

The improvement in morale is striking. Early discharge from the hospital effects an economy for the patient and an efficient utilization of beds by the institution. Prompt rehabilitation insures a minimal loss of time from work and the early re-establishment of normal activity.

HERBERT F. THURSTON, M.D.

Raven, R. W.: The Surgical Complications of Typhus Fever. *J. R. Army M. Corps* 1944, 83, 119.

The author witnessed several interesting complications of typhus fever among the Arabs of North Africa and ascertained that a racial resistance to this disease existed. Thus it was noted that the Russians have a high resistance, the French a moderate one and the Rumanians a low resistance with a corresponding incidence in surgical and suppurative complications.

The surgical complications of typhus fever may be classified into 3 groups: infective, vascular and ocular. Infective complications are usually manifested by abscess formation in the cephalocervical region, the extremities, the chest, the abdomen, or the perineum. Cellulitis is usually a fatal complica-

tion, and 6 such complications resulted in 100 per cent mortality. Acute parotitis was reported in 48 cases. Treatment consisted of one or more small incisions over the most prominent site of fluctuation. Pus may or may not appear but the diminution of intracapsular pressure is of value. Instead of surgery, x ray therapy over the parotid gland, especially in the nonpurulent infections may be used as a substitute.

Other reported complications include inflammation of the buccal cavity, mandible, larynx, bones and joints. Vascular complications occur in large numbers. These include phlebitis, and gangrene of the extremities of the intestine and of the skin. Gangrene of the extremities is usually of the dry type and occurs during the first weeks of convalescence. It is probably caused by a progressive obliteration of the blood capillaries and arterioles commencing in the distal part of the limb. Cutaneous gangrene may occur in the skin of the scrotum, of the extremities, and at pressure points. Ocular complications are manifested by thrombophlebitis of the orbital veins, atrophy of the optic nerve, corneal ulceration or paralysis of the third and sixth nerves. The possibility of surgical complications should be borne in mind by the attending physician and treatment instituted early. BENJAMIN G. P. SHAPIROFF, M.D.

GENERAL BACTERIAL, PROTOZOAN AND PARASITIC INFECTIONS

Dowdy A. H., Sewell R. L. and Vincent J. G.
The Prophylaxis and Therapeutics of Clostridial Infections (Gas Gangrene). *Y. Fork State J. M.* 44, 44, 390.

The authors have studied over 1,500 dogs in which clostridial infections have been produced. The report is confined to the sulfonamides, penicillin, and pentavalent antitoxin as far as treatment is concerned. Of the 377 untreated control dogs 93.4 per cent died. The infectious agents were virulent cultures of the clostridia *perfringens*, *septicum*, *novyi* (strains) and *sordellii*. Mixed cultures of the inocula produced a great increase in virulence and the amount of infection had to be reduced. The presence of *staphylococcus aureus* was found not to be responsible for the increase in virulence of the inocula.

The drugs employed for prophylaxis were sulfadiazine, sulfathiazole, sulfanilamide, and penicillin. The blood levels of the different agents were determined before, during, and after administration. Sulfathiazole was the most difficult to maintain at the desired levels. A three-day treatment period was followed by seven days of observation.

With the clostridium *perfringens* there was a 15 per cent survival of the controls. With the clostridium *septicum* there were no survivals. With one strain of the clostridium *novyi* there was a 4 per cent survival and with the second strain there was none. There was a 12 per cent survival with the clostridium *sordellii*. With the 5 strains mixed there was a 6.6 per cent survival.

Sulfadiazine was the most effective prophylactic with 93 per cent survival in infections caused by the clostridia *perfringens*, 72 per cent survival in those caused by clostridium *septicum*, 80 per cent in those caused by clostridium *sordellii*, but only 4 per cent in those caused by clostridium *novyi*.

Sulfathiazole was next in effectiveness and then sulfanilamide. The clostridium *novyi* proved extremely resistant to the action of the sulfonamides. The prophylactic experiment in which 7 dogs were treated with penicillin against the clostridium *novyi* showed a 73.4 per cent survival.

Therapeutically the experiments were carried out against 7 infectious agents except in the case of the sulfonamide resistant clostridium *novyi*. Sodium sulfadiazine, penicillin, and pentavalent gas-gangrene antitoxin, or a combination of these agents were used. Auxiliary sulfadiazine was used so that it would act directly on the invading organisms when antitoxin was the definitive agent. In order to simulate battlefield conditions more closely, the wounded should have received the prophylactic treatment with sulfonamides before they reached the base hospital for the definitive treatment.

The dosage of penicillin for a treatment was from 25,000 to 50,000 units per kilo of body weight. Massive doses of antitoxin over a short period of time were deemed preferable. The results showed that with sodium sulfadiazine used individually as the therapeutic agent against the mixed infection of clostridia *perfringens septicum*, *sordellii*, and *staphylococcus aureus*, there was a 48 per cent survival as compared to a 6.6 per cent survival in the control group. Against the same infection, when penicillin was used, there was a 100 per cent survival. Penicillin was used for therapeutics only with sodium sulfadiazine as the auxiliary agent. When penicillin only was used three hours after inoculation, 25 dogs showed a 100 per cent survival. When it was used six hours after inoculation along with sulfadiazine there was an 88 per cent survival. When it was used twelve hours after inoculation along with sodium sulfadiazine there was only 8.3 per cent survival, and when it was used with sulfadiazine three hours after inoculation there was 100 per cent survival.

Penicillin was used alone twelve hours after inoculation with no survivals. The antitoxin-penicillin combination was apparently the best treatment in the advanced stages of the infection.

The survival rates are higher for the sulfadiazine-treated animals than for the sulfathiazole-treated animals. In prophylaxis sulfadiazine is the best of the three sulfonamides employed when it is given systemically in such amounts as to maintain an adequate blood level. When the contaminating organism is the clostridium *novyi*, little or no protection can be expected from any of the three sulfonamides studied. Penicillin is of little value for prophylactic treatment and could not be used routinely under battle conditions. The authors did not test the prophylactic use of the pentavalent antitoxin.

Therapeutically when gas gangrene is apparent clinically sulfadiazine should be expected to be 50 per cent effective. It is suggested that it might be best to give the initial dose intravenously in the form of sodium sulfadiazine in order to obtain therapeutic concentration of the drug in the blood. Penicillin is much superior to sulfadiazine as a therapeutic agent as it is effective against the clostridium novyi as well as the other three clostridial organisms.

Penicillin should be extremely valuable early in the disease but it becomes less valuable as toxicity progresses. Pentavalent gas-gangrene antitoxin when used in large amounts and given early is very effective. In patients in whom the condition was far advanced and toxic the last agent was the only method found to be effective and if supplemented by sulfadiazine or penicillin it became very effective. The total amount as determined should be administered within eight hours at intervals of not more than two hours.

Clinically the patient should be tested for sensitivity to the antitoxin and if sensitive, carefully desensitized. Sulfadiazine or penicillin may be used during this desensitizing period.

Experimentally no contraindications were found to the combination of all three of these drugs.

It was suggested that surgical amputation should be indicated by the state of the vascular bed and not by the infection. RICHARD J. BENNETT JR. M.D.

Quill, L. M. and Burch, J. C.: Surgical Manifestations of Coccidioidomycosis. *Ann Surg* 1944, 120: 670.

Coccidioidomycosis occurs in 2 forms localized and disseminated. The primary or localized form has been referred to as San Joaquin fever, Valley fever and desert rheumatism. It is endemic in certain areas and regions of the Southwest. The causative organism has been shown to be a fungus. There are 2 phases in its life cycle: a vegetative and a parasitic. In tissue the organisms appear as double-contoured spherules of variable size containing endospores. The appearance of these spherules is characteristic, and their presence is diagnostic of the disease. Microscopically the growth is composed of interlacing mycelia with tiny chlamydospores attached to the aerial hyphae. Infection in the primary form is the result of inhalation or rarely inoculation of the chlamydospores which have grown out on the soil. It is unlikely that the disease can become established in new areas by the migration of infected persons. Man to man contact transmission is unknown. The parasitic spherule is not very infectious and must first grow as the vegetative form. It is pointless to isolate patients with the disease but care should be taken in the disposal of sputa and dressings.

The secondary form, or coccidioidal granuloma, is much rarer. It occurs about once in every 300 or 400 primary cases. It is due to a failure of the host to localize, or keep localized, the primary infection. Development of the granulomatous form usually

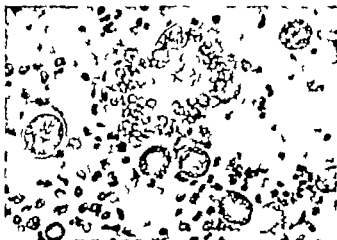


Fig. 1. *Coccidioides immitis*. Photomicrogram of the organism in tissue. (Courtesy of J. B. Lippincott Co.)

occurs quickly but occasionally the interval may be years.

The primary infection is commonly accompanied by signs and symptoms of a mild respiratory infection usually bronchitis with a productive cough. There may be chills, fever, anorexia, malaise, back ache and joint pains. Within the first eighteen days, erythema nodosum appears in 1 to 15 per cent of the cases. The leucocyte count is variable. Eosinophilia occurs late fairly regularly in the disease. The sedimentation rate is elevated. The sputum contains the diagnostic spherules during the active stage. If not found the sputum may be cultured. X rays may reveal only transient changes in the lungs. Exudative lesions may be associated with cavitation. The cavities are usually single and have a tendency to persist. Cavitation is the only lesion of surgical interest occurring in the primary phase.

Once the primary infection has been localized a high degree of immunity develops. Patients react to an extract of the organism somewhat as to tuberculin. This coccidioidin test depends on a skin sensitivity to a polysaccharide substance combined with a nitrogenous radical, and is an allergic manifestation. The usual dilutions used are 1:1000 and 1:100. The test is read at twenty-four, forty-eight and seventy-two hours. It is relatively disease specific. There is also a complement fixation test and a precipitin reaction.

When the infection is overwhelming or the resistance inadequate dissemination occurs. Any tissue of the body can be involved except the gastrointestinal tract. The individual lesions are usually granulomatous cold abscesses. A variety of surgical conditions can thus be simulated. Several cases are reported to illustrate the clinical similarity of coccidioidal granuloma and certain common surgical conditions such as appendicitis, Pott's disease of the spine and pneumonia. Cases simulating cord tumor, cerebellar abscess and peritonitis have been reported.

The prognosis is grave. In coccidioidal granuloma surgical removal if possible is probably the procedure of choice. Drugs such as colloidal copper tartar emetic, iodides, sulfonamides and penicillin have been found to be ineffective. Recently immune transfusions have been used with beneficial results in some instances. The pulmonary cavities are best treated conservatively. If hemoptysis is severe pneumothorax has given good results.

SAMUEL KARM, M.D.

DUCTLESS GLANDS

Kahn, J., and Stock, R. P.: Fatal Agranulocytosis Resulting from Thiouracil. *J Am M Ass* 944: 26-358.

Leucopenia and granulocytopenia have been reported as potential dangers in the use of thiouracil when given to thyrotoxic human beings. Similar observations have been made on adult rats which were fed thiourea. A white woman, age sixty-two, was admitted to the hospital because of nausea, drowsiness and vomiting of six hours duration. She was known to have had diabetes for six years and to have been negligent both in taking insulin and in following the prescribed diet. Diffuse goiter of relatively mild toxicity had been present for about ten years. On this admission to the hospital the patient was in impending diabetic coma. The response to therapy directed against acidosis was prompt. Because of the unstable nature of her diabetes, wholly satisfactory control never was possible.

As soon as possible after diabetic acidosis had been corrected, evaluation of the patient's thyrotoxicosis was made. Exophthalmos was slight. A fine tremor of the hands was present. A labile pulse varied between 100 and 120 pulsations per minute. The basal metabolic rate on the eleventh day was plus 65 per cent on two determinations. Blood cholesterol was 164 mgm. per 100 cc.

Thiouracil was started with an initial dose of 0.8 gm. per day in 4 divided doses for two days. Thereafter the amount was dropped to 0.6 gm. per day in 3 divided doses. A favorable response to thiouracil was prompt. The basal metabolic rate had dropped in fourteen days to plus 43 per cent. The patient had gained 4 lb. and the pulse rate was 80 per minute. The response to thiouracil continued to be favorable with a gradual rise in body weight and progressive lowering of the basal metabolic rate.

On the forty-fourth day of medication with thiouracil the basal metabolic rate was plus 10 per cent and the pulse stable at 80 pulsations per minute. At this time the dosage of thiouracil was reduced to 0.4 gm. per day. Seven days later the patient suddenly complained of a swollen, dry throat and within twenty-four hours her rectal temperature rose to 95 degrees. The erythrocyte count at this time was 3,650,000 and the leucocyte count had fallen to 1,100 per cubic millimeter with 3 per cent neutrophils, 1 per cent eosinophils, and 97 per cent lymphocytes. Thiouracil was stopped immediately. A total of 30.8

gm of thiouracil had been given over a period of fifty-four days preceding the clinical development of agranulocytosis.

The patient died five days after the appearance of agranulocytosis. At autopsy the bone marrow of several ribs and bodies of the vertebrae was abundant and dark red. Microscopically the cells of the granulopoietic series appeared to be greatly reduced in number. The clinical diagnosis of both diabetes mellitus and toxic diffuse goiter was supported by the anatomic findings. Death in this case was doubtless due to the agranulocytosis with its subsequent agranulocytic angina. HAROLD C. OCHSNER, M.D.

Frame, E. G., Fleischmann, W., and Wilkins, L.: The Influence of a Number of Androgenic Steroids on the Urinary Excretion of Neutral 17-Ketosteroids. *Bull Johns Hopkins Hosp* 944: 75-95.

The authors' study confirms the results of previous investigators on the effects on 17-ketosteroid excretion of the administration of different androgenic steroid and presents the results of the administration of 4 additional steroids which have not hitherto been reported. The use of dwarfed, sexually retarded boys with very low urinary 17-ketosteroids before treatment as subjects affords certain advantages in that the possible complication of obscuring the effect of steroid administration by lowering the body's production of 17-ketosteroids is reduced to a minimum.

Eleven different steroids having an androstane or androstene nucleus were administered to sexually underdeveloped dwarfed boys ranging in age from nine to eighteen years and the effects on the neutral 17-ketosteroid excretion were determined.

The administration of the following compounds was accompanied by a significantly increased excretion of 17-ketosteroids: testosterone (free or propionate), androstosterone, dehydroisandrosterone, Δ^4 -androstenedione-(3,17), Δ^5 -androstenediol-(3 β ,17 α)-diacetate and androstenediol-(3 α ,17 α)-diacetate.

The authors conclude that for this reason the 17-alkyl androgenic steroids are valuable agents in the study of the effects of androgen administration on the endogenous production of urinary 17-ketosteroids.

JOSEPH K. NARAT, M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Symmers, D.: Clinical Significance of the Deeper Anatomic Changes in Lymphoid Dissem. *Irish Ind. M* 944: 74-164.

Anatomically, chronic lymphogenous leucemia is broadly divisible into two forms, a splenomegalic form, in which lymphoid hyperplasia is preponderant or 'primary' in the spleen, and a form in which the abdominal lymph nodes or the abdominal and thoracic nodes combined are preponderantly or 'primarily' enlarged. In both forms, enlargement of the superficial nodes if it occurs at all, is secondary. The same statement applies to Hodgkin's disease,

with the addition that in this disease there is a form that is preponderant or primary in the thymus and one that is preponderant or primary in the liver. In giant follicular lymphadenopathy the preponderant or "primary" changes are most often in the lymph nodes of the abdomen. It is probable that there is a preponderant or primary splenomegalic form, but proof of this awaits confirmation by evidence adduced at necropsy. In the majority of all cases of lymphosarcoma (70 per cent) the preponderant changes are in the gastrointestinal tract in the thymus or in the abdominal or the thoracic lymph nodes rarely in the spleen. Enlargement of the superficial lymph nodes if it occurs at all is usually a later and secondary feature. The gastrointestinal so-called "pseudoleucemia" of Briquet, as its name implies, is preponderantly or "primarily" a disease of the lymphoid tissues of the gastrointestinal tract. Splenomegaly and enlargement of the superficial and deep lymph nodes, while almost constantly present, are secondary features. The distribution of the lesions in the lymph nodes of the thorax and abdomen seems to warrant the view that the causative agent of each of the lymphoid diseases enters through mucous membranes most often through the mucous membrane of the gastrointestinal tract. In other circumstances, it appears that the causative agent filters through both the mucosal follicles and the lymph nodes in the abdomen and chest, and eventually brings about hyperplastic changes in the follicles of the spleen in the thymus or its remains or in the auxiliary lymphoid foci scattered through the interstitial tissues of various organs.

Stemmerman M. G. and Auerbach, O.: The Value and Limitations of the Congo-Red Test for Amyloidosis. *Am. J. M. Sc.*, 1944 308 305.

The results of 649 Congo-red tests for amyloidosis performed on 446 patients have been reviewed in order to evaluate the test and to determine the sources of error. It has proved to be a valuable procedure, in spite of a certain proportion of erroneous results, which in the authors' series has been calculated as 24.3 per cent of false negatives and 4.2 per cent of false positives.

The presence of only minimal amounts of amyloid is the principal reason for false negative results, while technical errors are probably the chief cause of false positive reports.

The determination of the presence of Congo red in the urine within one hour after injection of the dye has been of little value in the diagnosis of amyloid nephrosis.

HAROLD C. OLSBERG, M.D.

Howe, C. W., and Warren S.: Myoblastoma. *Surg.* 1944 16 319

One of the less well recognized tumors is the myoblastoma, the type cell of which is the primitive precursor of striated muscle. Myoblastoma must be differentiated from other primitive tumors of mesenchymal type on the one hand and from rhabdomyoma and rhabdomyosarcoma on the other hand.

The two chief types of readily recognized striated muscle tumors are those occurring in voluntary and those occurring in cardiac muscle. The latter are almost all congenital and benign.

The tumor is usually first noted as a small yielding nontender mass often only 1 cm. or more in diameter. On section it is grayish pink or whitish and as a rule it is fairly clearly demarcated although it occasionally shows no definite border. Ulceration is rare and, indeed, there may be hyperplastic or neoplastic response of the overlying skin or mucous membrane.

The authors have reviewed the clinical data and microscopic findings of 104 cases collected from the literature and present 10 new cases, 5 of which showed definite malignant properties, 3 of the latter metastasized to the lungs.

Fifty-six per cent of the cases reviewed occurred in the upper respiratory and digestive tracts. Fifty-nine cases occurred in the tongue and of these 3 (5 per cent) were malignant. Eleven per cent of the total cases were malignant and of these only 3 showed proved metastasis. Age had no clear influence on the occurrence of malignant myoblastic tumors. The patients ranged from eight to eighty-one years of age although 9 of 13 were over fifty years of age.

Whenever a myoblastoma is reported to have (1) atypism of cells (2) excess mitotic figures, (3) spindle-cell or sarcomatous pattern or (4) local invasion it should be treated surgically as a malignant tumor until more is known of the nature of these growths especially if the patient is over fifty years of age. The degree of radiosensitivity and frequency of metastasis are as yet unknown. Both appear to be low.

On the basis of available data, 37 patients were treated by surgical excision, 3 by excision and electrocoagulation, 5 by excision and radium therapy and 1 by electrocoagulation.

JOSEPH K. NAKAT, M.D.

Morehead R. P.: Carcinoma in Young Persons. *Arch. Path. Chic.* 1944 38 141

Neoplasia is a growth disturbance resulting in various types of tumors which appear at characteristic times of life. In infancy and early childhood are found adenosarcoma of the kidney, retinoblastoma and malignant neurocytoma. Histogenetically these tumors are embryonic in type and are related to some stimulus from a defect in the cells of the anlage. Late childhood or the presexual period of life has a very low incidence of neoplasia, which is indicative of exhaustion of the carcinogenic factor active in infancy. During puberty the various types of bone sarcoma attain their greatest frequency. This period of life is associated with the critical stages of osteogenesis which indicates a relationship of bone sarcoma with growth initiation factors and primitive connective-tissue rests.

The author emphasizes the importance of carcinoma in the young and claims that its significance

TABLE I.—DISTRIBUTION OF TYPES OF CANCER ACCORDING TO PERIODS

Infancy and early childhood	Adenocarcinoma of (kidney) Retinoblastoma Malignant neurocytoma of gland (adrenal)
Late childhood or preadult period	Fewer tumors appear than at any other period of life
Puberty	Sarcoma of bone Tumors of adult life begin to appear and those of childhood disappear
Young Ad. lt.	Precocious cases of adult tumors increase in number
Middle Life	Malignant lymphoma Carcinoma of cervix Carcinoma of breast Carcinoma corpus uteri Carcinoma of liver Carcinoma of stomach Carcinoma of rectum
Old age	

has been lost in the maze of generalizations. Only 15 cases of carcinoma of the cervix occurring at or below the age of twenty years are reported in the literature. The author has added 3 new cases to this number. Carcinoma of the cervix in the young indicates that age influences the morphology of cancer with the adenocarcinomatous type of malignancy predominating in more than two-thirds of the cases. Carcinoma of the body and fundus of the uterus was found in 3 patients under the age of thirty. Primary carcinoma of the liver is not unusually rare and has been found in 41 infants under two years of age. This suggests that congenital factors may be related to the etiology of cancer in the liver. Other carcinogenic factors may be hereditary or environmental.

In the discussion, Bask said that in an Army hospital, 4 soldiers under the age of thirty-five were found to have carcinoma of the stomach and 5 under twenty years of age had carcinoma of the large bowel. Clinically the young are not exempt or immune to neoplastic disease.

Rector said that in Michigan there were 546 deaths from cancer in persons under the age of twenty years during a five year period.

BENJAMIN G. P. SHATTUCK, M.D.

EXPERIMENTAL SURGERY

Gibson, S., Chese, D., and Cole, W. H.: Experimental Tourniquet Shock with Particular Reference to the Toxic Factor: A Method of Production Eliminating the Influence of General Anesthesia and Nervous Impulses. *Arch. Surg.* 1944, 49.

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Tourniquet shock can be produced consistently in animals and therefore it is particularly adaptable for study, but the extreme pain produced by the tourni-

quet makes it necessary to utilize some type of anesthesia. Prolonged anesthesia is undesirable. Moreover since nervous impulses are obviously so intensive this factor might alter the data derived from the experiment. To obviate these disadvantages the authors have adopted the procedure of cutting the spinal cord at the level of the lower dorsal or uppermost lumbar vertebra, from two to four days before the experiment is to be performed. Manipulation or operation may be conducted without pain on the lower extremities of the animal with no other anesthetic than a moderate dose of morphine. To keep the tourniquet anchored in one place a sterile nail is driven deeply into the trochanter. In the experiments in which shock is produced by the release of the tourniquet, death always occurred if the tourniquet was left in place for at least nine hours. In 10 animals studied by this method death occurred after an average period of two hours and thirty four minutes following release of the tourniquet. The average loss of plasma into the extremity before and following release of the tourniquet was only 2.1 per cent of the total body weight which is insufficient in itself to explain death.

To determine whether or not a toxin may be developed in the constricted limb and whether this may have been an important factor in the pathogenesis of shock and death, the authors performed a cross transfusion by injecting blood obtained from the distal portion of the femoral vein of the constricted limb into a normal animal. To prevent increase in shock in the animal subjected to the application of the tourniquet through loss of blood, an equal amount of blood was removed from the recipient dog and injected into the shocked animal.

Four of the 5 animals receiving blood from the constricted limb after release of the tourniquet died in from two to twelve hours after the transfusion was begun. The only dog to survive transfusion of blood which had circulated through the constricted limb was one which did not receive any blood from the constricted limb until ten minutes following the release of the tourniquet. If a toxin was present in the constricted limb it would supposedly be more concentrated in the blood draining from the limb during the first few minutes following release of the tourniquet. If this were true, survival of the animal (which however did go into shock during the transfusion but recovered afterward) might be explained.

HOWARD A. McKNIGHT, M.D.

Duncan, G. W., Irvin, J. L., and Sarnoff, S. J.: Non-protein Nitrogen and Protein Concentrations in the Serum and Cerebrospinal Fluid in Shock. *Bull. Johns Hopkins Hosp.* 1944, 75, 35.

Several investigations of problems related to shock have directed attention to possible alterations in the permeability of the membranes, particularly capillary membranes located at the site of the trauma or in more general regions. Although the barrier relationship between the blood and cerebrospinal fluid

differs considerably from that existing between the blood and interstitial fluid the cerebrospinal fluid is easily accessible and may reflect some of the general relationships and certain changes which occur in shock. The problem was approached by the authors by a comparison of the nonprotein nitrogen and protein concentrations of the serum and cerebrospinal fluid during experimental shock.

The type of shock which appeared to be most suitable for this study was that produced by experimental crushing injury, since it has been shown to be characterized by low blood pressure, progressive hemoconcentration, evidence of renal damage and death unless treatment is instituted. Fourteen dogs were used as experimental animals. Anesthesia was produced by subcutaneous injections of morphine and nembutal. The mechanical press was applied to a thigh of the animal for a period of fifteen hours at a pressure of approximately 500 pounds. At the end of this time the press was removed and the animal was observed until the arterial pressure had declined to a level between 50 and 60 mm. of mercury. In most instances an attempt was made to maintain the animal in shock for the maximum period which still would allow time for the collection of specimens of blood and cerebrospinal fluid before death occurred.

The animals of the control group were given the same amount of anesthetic and were restrained on the table for a period of time equal to the experimental periods for the animals in which shock was produced.

All of the 14 animals subjected to crushing injury demonstrated progressive evidence of shock following the removal of the press at the end of a period of fifteen hours. There was progressive swelling of the injured thigh, progressive fall in the arterial pressure, progressive hemoconcentration and evidence of renal damage. The time of collection of specimens of cerebrospinal fluid and blood, after the development of severe shock, varied from three to eight hours after removal of the press. The collection of cerebrospinal fluid specimens from animals in shock was more difficult than the collection from the control group and at autopsy the ventricles and the spinal subarachnoid space showed gross diminution of fluid in a majority of the cases.

The mean concentrations of both nonprotein nitrogen and protein in the serum and cerebrospinal fluid were found to be significantly greater in the animals in which shock was produced.

From the standpoint of the objective of the authors' investigation the distribution ratios for nonprotein nitrogen for the two groups suggest that gross alteration of the barrier relationship between the blood plasma and cerebrospinal fluid did not occur under the conditions of these experiments. The small but significant increase in the distribution ratio during shock may be explained reasonably as being due to a lag in the normal transfer and distribution of nonprotein nitrogenous substances across the barrier. The increase of the mean concentration of protein in the cerebrospinal fluid of the animals in

shock may be explained on the basis of a slight shift of water from the spinal fluid resulting from the hemoconcentration.

The mean ratios of the concentrations of nonprotein nitrogen in the serum to the corresponding values in the spinal fluid were 1.58 for the control group and 2.02 for the group of animals in shock. The mean ratios of the concentrations of protein in the serum to the corresponding concentrations in the cerebrospinal fluid were essentially the same for the two groups.

The experiments indicate that if alteration in the barrier relationship between the plasma and cerebrospinal fluid does occur in shock produced by this method it is not sufficient to permit extensive passage of the plasma proteins into the spinal fluid.

JOSEPH K. NARAT, M.D.

Bialock, A.: Utilization of Oxygen by the Brain in Traumatic Shock. *Arch. Surg.* 1944, 49: 167

Reduction in the effective volume of circulating blood in traumatic shock results in varying degrees of anoxia of the different structures of the body. The nervous system is probably more sensitive than other tissues to a deficit of oxygen and it is likely that irreversible changes take place there first. Many studies have been performed in recent years on the metabolism and blood flow in the kidneys, the liver, and other organs in shock. The brain has not received sufficient attention in this regard because of difficulties connected with methods for determining the cerebral blood flow and for collecting cerebral venous blood.

The author's studies on dogs consisted of determinations of the oxygen content of arterial blood of the oxygen content of venous blood obtained from the confluence of cerebral sinuses and of the total oxygen consumption of the animal after shock was produced by several different methods. The author appreciated at the initiation of these experiments that changes in the arteriovenous oxygen difference may not parallel alterations in the cerebral blood flow. At the same time it was hoped that information on the cerebral utilization of oxygen and the total oxygen consumption of the body would shed some light on the manner in which the brain responds to a reduction in blood volume, cardiac output and arterial blood pressure.

All of the four experimental conditions for producing shock—hemorrhage, trauma, tourniquets and burns—were associated with an increase in the arteriovenous difference of both the cerebral sinus blood and the mixed venous blood. The oxygen utilization of the cerebral sinus blood and that of the mixed venous blood, in general paralleled each other closely. The difference in oxygen content of the arterial blood and that of the sinus blood increased in the early stages of shock and this difference usually became more marked as shock developed. The early increase in the arteriovenous sinus-oxygen difference was due in some instances to an increase in the oxygen content of the arterial blood rather than to a

decrease in oxygen content of the venous blood. Alterations in the total oxygen consumption of the body throughout the course of the experiments were of great. If one could assume that the oxygen consumed by the brain also remained essentially constant, the finding of an increased utilization of oxygen would mean that the cerebral blood flow was considerably reduced. Such an assumption is not warranted.

It appears that under conditions of decreasing blood flow the brain unlike the kidneys can maintain its oxygen consumption at least partially by extracting increased proportions of oxygen from the arterial blood.

JOSEPH K. NARAY M.D.

Soto, M.: Experimental Observations on Traumatic "Shock" and a Study of the Action of Remedies in this Condition (Observaciones experimentales sobre el shock traumático y estudio de acciones medicamentosas en el mismo) *Presencia med. argent.* 1944, 3, 143.

The author reports an experimental study of shock and the effect of remedies used for it. Dogs were used as experimental animals, and shock was brought about in two ways—by opening the abdomen and exercising traction on the rectum and gall bladder and by bringing the intestines outside of the abdomen and wrapping them in compresses wet with physiological salt solution. If the animals were subjected to either of these procedures until the blood pressure fell to half its normal value they never recovered spontaneously. The author used various remedial agents after the shock had reached this stage and presents graphs showing the pulse in different stages of shock and after the remedies were administered.

He gave physiological salt solution and glucose solution in doses of 20 cc. per kilogram of weight these were repeated 4 times at intervals of an hour. This brought the blood pressure up temporarily but did not save the animals. Salt solution seemed to have a better effect than glucose solution. Hypertonic solution seemed to have a less favorable effect than isotonic solution. Sympathetic stimulants such as ephedrine, adrenalin, veratril and benzadrine had about the same effect as in normal animals except that it was less pronounced and shorter in duration. The effect was not visibly improved by giving the stimulant in salt or glucose solution. Atropine as an inhibitor of the vagus was used without any markedly beneficial effect. Caffeine, as a stimulant of the central nervous system was given up to convulsive doses without any perceptible effect. Although most authors insist that digitalis

preparations are ineffective in shock because the circulatory insufficiency is due to decrease of volume and not to heart failure, it was found that the derivatives of digitalis and strophanthus dissolved in salt solution had appreciable effects and prolonged the life of the animals. The best results were obtained with a hypotonic solution of sodium glycerophosphate to which a digitalis preparation was added. This improved the condition of animals which were in a worse condition than those helped by moraine solutions and preserved life longer, but none of the remedies saved animals that had reached a certain stage of shock. The digitalis increases the resistance of the heart to fatigue and the hypotonic solution causes a hemolysis which sets free hemoglobin, phosphatides and other substances that have a good effect.

AUGUST G. MOORE, M.D.

Ireneau, C. Jr., and Puestow C. B.: The Effect of Massive Experimental Hemorrhage on the Hepatic Function in Dogs. *Arch. Surg.* 1944, 4, 60.

Experiments were performed in order to determine whether or not massive hemorrhage could produce enough damage to the liver to give rise to hepatic insufficiency. Twelve dogs were bled from the jugular vein predetermined amounts of blood being withdrawn every five minutes for thirty minutes so that the amount of blood removed was 30 cc. per kilogram. This amount of blood loss constitutes a sublethal hemorrhage. The hepatic function tests employed were the sulfobromophthalcin sodium (bromsulphalein) test, the galactose tolerance test, the prothrombin time test and the serum phosphatase test.

The galactose tolerance test consistently showed results indicative of hepatic damage, the excretion of galactose being above normal in 8 of 11 animals. The prothrombin time was definitely prolonged in 4 of the 11 animals. The other tests gave results within the limits of normal.

The authors point out that if one or two tests of hepatic function give positive results, a certain amount of hepatic insufficiency exists, since the tests are so insensitive that a positive result must be considered significant. The wide margin of safety possessed by the liver, only from 30 to 40 per cent being necessary to maintain life is possibly the explanation for the mild impairment of hepatic function found in these experiments.

It is concluded that definite although slight impairment of hepatic function was produced by massive acute hemorrhage in these experiments.

JOHN L. LUDWIG, M.D.

March, 1945

International Abstract of Surgery

*Supplementary to
Surgery, Gynecology and Obstetrics*

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INTERNATIONAL ABSTRACT OF SURGERY

VOLUME 80

MARCH, 1945

NUMBER 3

ABSTRACTS OF CURRENT LITERATURE SURGERY OF THE HEAD AND NECK

EYE

Callahan, A.: Eye Injuries at an Aircraft Plant.
J M Ass Georgia, 1944, 33 312

A series of 404 eye injuries observed between January 1942 and October 1943 is presented, with an evaluation of some of the clinical and therapeutic problems encountered in industrial ophthalmologic practice at an aircraft plant

In most instances the traumatic agents in these cases were particles of concrete or similar material or of various types of metals aluminum and light alloys in particular used in the construction of airplanes

Early recognition and treatment are imperative in all ocular injuries because the tendency of many reparative processes in the eye is toward the formation of nontransparent tissue. In this series when the injury did not respond to adequate local therapy syphilis was suspected and found responsible in a great number of cases. The average man hour loss resulting from eye injuries was appreciably decreased when pre-employment examination and serologic tests were used to rule out those individuals with physical defects and systemic diseases such as syphilis.

A technique was devised by which the patient's head was fixed firmly against the chin rest and forehead bar of the slit-lamp microscope. Analgesia was produced by 1/2 per cent pantocaine. Dissection and removal of all embedded particles with various spuds were done under direct observation with the (20X-40X) microscope.

Scant attention has been paid heretofore to a chemical sensitivity of the eye structure to aluminum compounds. However most of the cases listed under traumatic and chemical conjunctivitis were those in which small particles of this metal were adhering to the surface of the conjunctiva.

Only 3 eyes were totally lost in the entire series of cases.

Two case reports of intraocular foreign bodies are given in detail, with illustrations concerning their extraction.

LESLIE L. MCCOY M.D

Marshall J. C.: A Case of Polycythemia Vera Extraction of Both Lenses with a Satisfactory Result *Brd J Ophth*, 1944, 28 481

The case of a seventy four year-old man with cataracts and a diagnosis of polycythemia vera in which the lenses were successfully extracted, is reported in detail. A previous examination had shown the presence of retinal hemorrhages in the left eye, but in spite of this vision of 6/6 was obtained in each eye with correction after surgery

The author concludes that it is justifiable to carry out surgery in cases of polycythemia vera if it is required. Even in severe cases the retinal lesions may return to normal or leave minimal damage. Fundus examination in some cases may cause confusion with cerebral tumors because of the edema of the optic discs

WILLIAM A. MANN M.D

Asbury M. K. Epithelial Tumors of the Iris.
Am. J Ophth, 1944, 27 1094

Four epithelial tumors of the iris are described in detail, including a previously reported in the literature. The author describes these as a group of relatively benign epithelial tumors which affected principally the iris and arose presumably from the posterior iris epithelium or the anterior edge of the ciliary epithelium. They were circumscribed but not encapsulated with a wide variation in pigmentation. In spite of the benign histological characteristics there was a definite tendency toward local invasion and destruction. They might be classified as medulloepitheliomas or perhaps as a group between truly benign epithelial hyperplasia and malignant epithelioma.

WILLIAM A. MANN M.D

EAR

Matthews, R. M. S. Obstruction of the Eustachian Tube and Barotrauma in Air Crews. *Brd M J*, 1944, 2 523.

Obstruction of the eustachian tube and otitic barotrauma present one of the greatest problems of the medical officer on a flying station. The term

eustachian obstruction" is used to represent all degrees of impaired patency up to complete block while otitic barotrauma refers to those cases presenting persistent abnormal drum appearances and hearing changes. The anatomic arrangement of the tubes is such that on ascent the relative increase of pressure in the middle ear is relieved spontaneously at definite intervals. On descent however spontaneous equalization of pressure does not occur and voluntary effort is necessary to allow air to enter the collapsible pharyngeal opening. This is done by swallowing and sometimes by manipulating the mandible by wide chewing movements or by auto-inflation. Eustachian obstruction causes a sensation of blocking of the ears, and the drum may be slightly invaginated in appearance. If the man has discovered his condition through flying there may be barotraumatic changes as well. On attempting auto-inflation no movement is observed and no subsequent click is heard. The determination of whether the tubes are patent may be a problem since normally movement of the drum is not always visible on auto-inflation nor is there always an audible click. The presence of a cold does not always cause tubal obstruction and mild forms of chronic rhinitis, pharyngitis and tracheitis do not necessarily curtail flying duties. Otitic barotrauma is indicated at first by a sensation of fullness then increasing deafness and lastly pain. In slight cases the drums appear invaginated and injected with slight impairment of hearing. In moderate cases hemorrhagic areas appear in the drum and in these recovery takes longer. In severe cases an effusion may occur into the middle ear and in rare cases there may be rupture of the drum.

Prevention is of greatest importance. The time spent by the medical officer in instruction of the flying personnel is well repaid.

The treatment used for eustachian obstruction consists in the instillation of 3 drops of $\frac{1}{4}$ per cent ephedrine in liquid paraffin in each side of the nose while the patient is in the horizontal position with the head dorsiflexed on the neck until the tip of the chin and the ear are in the same vertical plane. After three minutes auto-inflation is attempted. There have been no cases of spread of infection to the middle ear. Inhalations of menthol and eucalyptol in hot water are used afterward. If relief is obtained the man is limited to nonoperational duty for one night. If the tubes are still not patent after treatment the patient is confined to ground duties. The average time for recovery to fitness for full flying is two and five-tenths days. Benzadrine and karsodrine inhalers are convenient for air crews and are used before and after descent. Otitic barotrauma is most satisfactorily relieved by immediate ascent to a height above that at which barotrauma began and subsequent slow descent with frequent auto-inflation. On landing, treatment is necessary at the earliest opportunity the first essential being to obtain patency of the tubes. If the use of a vasoconstrictor and Valsalva's method is unsuccessful, politizeriza-

tion is used. Catheterization is seldom needed. The effects of the trauma must be resolved before flying is resumed. In the cases referred to this required an average of twenty and four tenths days.

JOHN R. LINDSAY, M.D.

Ullmann, E. V.: Traumatic Deafness in Combat Flyers. *Arch. Otolaryng. Chlc.*, 1944, 40: 174.

A total number of 900 officers and 1,355 enlisted flying personnel were examined after combat duty. Of this series 100 officers and 40 enlisted men are given special examination of the acoustic mechanism. These men were between the ages of twenty and thirty years. There was no complaint about their ears on questioning except an occasional humming and ringing in one or both ears. There was no trauma to the drums. Of this series only 3 officers showed no damage to the acoustic mechanism, while 97 showed definite changes. Three per cent showed a loss of 100 decibels in one or more frequencies; 71 per cent showed a loss of 50 decibels in one or more frequencies; and 12 per cent a loss of from 10 to 25 decibels in one or more frequencies. In 6 cases the damage was traced to the middle ear.

Sixty six per cent of the officers showed a fatigue notch at frequency 2,806. 16 per cent at 4,000, and the remaining 18 per cent had mixed forms of hearing loss in which the original fatigue notch could no longer be distinguished. The time which had elapsed between the last flight and the audiogram was from ten to six weeks.

JOHN F. DUNN, M.D.

Swanson, C. A., and Baker, D. C., Jr.: The Use of Penicillin in Diseases of the Ear. *J. Am. A. O. A.*, 1944, 36: 616.

The Penicillin Committee at the National Naval Medical Center believes that the intramuscular administration of the drug is the most practicable. In order to insure the therapeutic effectiveness of the drug, this Committee stresses the importance of two conditions:

1. The maintenance of adequate nutrition and a positive nitrogen balance in patients who are receiving the drug.

2. Accurate preliminary bacteriologic studies to determine that the pathogen is an organism susceptible to the drug.

Infectious diseases of the ear can be effectively treated with penicillin because the anatomic structure of the ear permits the local administration of the drug and because the organisms causing most acute infections of the ear are usually in the group believed to be susceptible to the drug. Fowler made a study of 452 consecutive cases of acute otitis media. If his statistical analysis of the causative organisms in that series is correct, then 90 per cent of the organisms are susceptible to penicillin.

In this study the sodium salt was used. It was given by continuous intravenous injection, intramuscular injection or local instillation. In 1 instance a combination of the intramuscular and local routes was used.

The author summarizes his article as follows:

In acute otitis media penicillin is administered by intramuscular injection. The amount of drug necessary depends on the causative organism and the severity. Staphylococcal infections usually require a greater amount than those due to streptococci. The drug should be continued after the patient seems well to avoid possible relapse.

When surgical intervention is done in acute mastoiditis it can be supplemented by penicillin administered either intramuscularly or by local instillation into the mastoid cavity. In 1 case, penicillin seemed to shorten convalescence and hasten recovery from facial paralysis.

In acute labyrinthitis penicillin can be administered by the continuous intravenous injection method.

Special cases of chronic otitis media can be treated successfully by the local instillation of penicillin into the middle ear. The patients best suited to this therapy are patients with chronic discharging ears caused by organisms susceptible to penicillin and with large perforations of the drum with no evidence of granulations or cholesteatomas. The pneumatic otoscope is good to force the drug into the middle ear and the penicillin can be sealed in by means of cotton impregnated with a bland ointment.

LUCIAN L. MCCOY, M.D.

Kellemen, G.: Fractures of the Temporal Bone. *Arch. Otolaryng., Chic.* 1944, 40: 333

The author presents a collection of 80 photomicrographs covering a series of 18 deaths due to skull fracture involving the temporal bone. These deaths occurred from trauma induced by moving vehicles and falls from high places.

For comparison, photomicrographs taken in cases of craniotomy for delivery are included. The pictures dealing exclusively with human material demonstrate the variations of temporal fractures with their effects on the different component tissues of the external middle, and internal ear.

After the usual fixation, decalcification and embedding, the sections were cut chiefly in the horizontal plane, with the exception of a small group which were cut vertically. All were stained with hematoxylin-eosin.

JOHN F. DILLON, M.D.

NOSE AND SINUSES

Butler, D. B., Greenwood, G. J., and Ivy, A. C.: Reduced Atmospheric Pressure as a Form of Treatment for Paramaxillary Sinusitis. *Arch. Otolaryng., Chic.*, 1944, 40: 366.

The authors state that of 125 patients who were treated for chronic sinus disease in a high-altitude chamber by rapid decompression of the atmospheric pressure to 523.6 mm. of mercury 89.5 per cent experienced subjective improvement at the conclusion of their course of treatment.

Of 29 patients who were followed up by serial roentgen studies after the instillation of radio-

opaque oils 17 (58.6 per cent) showed improvement in the roentgenogram after the decompression treatments.

Of 42 patients who were studied by repeated rhinologic examination, 30 (71.4 per cent) showed improvement in their sinus condition after being treated by decompression.

A total of 2,259 treatments were given. The average number per patient was 18.1.

Decompression therapy is a simple nontraumatic form of treatment for subacute and chronic sinus disease.

JAMES C. BRASWELL, M.D.

Putney, F. J.: Uses of Penicillin in Diseases of the Nose and Throat. *J. Am. M. Ass.* 1944, 126: 620.

The author presents 9 cases of sinus diseases in which penicillin was administered because life was endangered. It was found that acute conditions responded better than chronic ones. In chronic cases the infection often became active after treatment was terminated. Failure to respond to penicillin is attributed to resistance of the organism to the drug. The author believes that if the condition shows no improvement and the purulent drainage continues after three or four days of penicillin therapy sensitivity tests should be performed. Osteomyelitis still requires surgical intervention which is best performed during the period in which the infection has been checked by penicillin. This drug is effective against sulfonamide resistant organisms and cases which had had sulfonamide therapy were as much improved by penicillin as those which had not been treated with sulfonamides. There were no toxic reactions systemically or locally. Penicillin was used in 6 cases of osteomyelitis (of the frontal bone in 5 cases and of the frontal and maxillary bones in 1 case) and in 3 cases of orbital cellulitis secondary to sinusitis. In chronic osteomyelitis penicillin therapy for several months may prevent the need for extensive surgery. Brain abscess or intracranial abscess and orbital cellulitis occurred in 3 cases of osteomyelitis without any relation to the response to the drug.

In addition to the local use of penicillin 24,000 units were given intramuscularly every three hours followed by 15,000 units every three hours when the condition improved.

Prompt healing occurred, but the underlying sinusitis was unaffected in 3 cases of orbital cellulitis; sinus surgery was necessary in 2 cases. These patients had been given sulfonamide therapy previously without improvement.

In 1 case of cavernous-sinus thrombosis death occurred on the eleventh day of therapy. 400,000 units of penicillin had been given in the first two days by continuous intravenous drip and this was followed by 25,000 units given intramuscularly every three hours thereafter.

Acute infections of the maxillary sinuses have been cured after several irrigations with a solution of 250 units of penicillin per cubic centimeter. In Vincent's infection of the mouth and of the tonsils the

organisms disappear after a few days of systemic penicillin therapy.

In discussing this article VORSTER recommended a solution of 500 units per cubic centimeter for gonorrheal ophthalmia. 4 drops of this solution to be instilled every hour. Smears and cultures from the conjunctiva became negative after twenty-four hours and there were no recurrences. The penicillin should be continued until at least three consecutive daily examinations are negative.

Penicillin has also been used for irrigation of the lacrimal passages in cases of chronic suppurative dacryocystitis. A cc of the 500-unit solution are given daily. After the second irrigation the secretion usually becomes negligible and after several days it becomes clear.

KOENIG obtained good results in early acute dacryocystitis with 15,000 units of penicillin every three hours around the clock for seven days until the drum resolved and the landmarks returned. Then 10,000 units for three or four days and 5,000 units for three or four days more. HANSEN used heparin in conjunction with penicillin in carcinoma of the thrombosis. PEPPER emphasized the importance of surgery in lateral sinus thrombosis in conjunction with penicillin therapy. JOSEPH ZIEGLER, M.D.

ILGEN, F. Z. and Thornell, W. C.: Malignant Tumors of the Nasal Cavity. Report of 3 Cases in Which a Frontothmoid Approach was Employed. *Arch Otolaryngol* 1944 40 395.

Many methods of approach to the nasal cavity and paranasal sinuses have been devised for removal of benign and malignant tumors and for treatment of suppurative disease of the paranasal sinuses. The authors review various procedures that have been used since 1891 and describe a method of approach they have used with satisfaction in certain selected cases in which malignant disease was present but in which there was little or no roentgenological evidence of involvement of bone. They report 8 cases.

Carcinoma within the nasal cavity is most likely to be found on the septum or high on the lateral wall of the nasal passage. Recent nasal obstruction and increased nasal discharge or purulent discharge with bleeding should suggest the possibility of malignant disease. Although nasal obstruction is often attributed to polyps, recent nasal obstruction particularly when the patient is more than forty years of age is not likely to be due to polyps. Far too frequently such so-called "polyps" have been removed repeatedly without a suspicion of carcinoma and without pathological examination of the removed tissue. Such mismanagement allows carcinoma to advance until removal is impossible. If a mass in the nose bleeds readily on slight trauma or if its removal is followed by free bleeding, a malignant lesion should be suspected until some cause other than carcinoma has been found.

A carcinomatous mass which may not be primary in the nose may be found in a nasal passage. It may be an extension from the maxillary sinus or from the

ethmoid cells. Such a mass in the nose, whether or not it is primary, often is ulcerated and infected. This probably is due to trauma from crusting and perhaps is aggravated by the patient's efforts to clear the nostril. If a specimen is obtained for biopsy the instrument may remove only laminated necrotic portions of the tumor. Correct diagnosis on examination of such tissue is difficult or impossible. A negative report, therefore, must not be accepted with complete assurance until it is certain that a representative specimen has been examined by the pathologist.

Roentgenograms of the paranasal sinuses are essential in cases of tumor. In a number of the author's cases the sinuses appeared cloudy on the side on which the lesion was situated and clear or comparatively clear on the opposite side. This finding suggests obstruction due to neoplasm rather than an inflammatory process. Erosion of bone indicates extension of the malignancy beyond the nasal mucosa. The final diagnosis rests on biopsy. Determination of the degree of malignancy by grading according to the method of Broders is of great aid in deciding on the best plan of treatment.

Treatment of malignant disease within the nasal cavity when the roentgenogram reveals little or no evidence of involvement of bone requires adequate exposure (1) to ascertain the extent of the tumor and to find its point of attachment, (2) to permit proper control of hemorrhage and (3) to permit removal of the tumor and if necessary accurate implantation of radium. In some of the author's cases, the tumor, although large, was attached by a narrow pedicle. Without adequate exposure it would have been impossible either to ascertain this or to carry out accurate removal.

The incision is started just under the unshaven eyebrow, 1 cm. lateral to its inner extremity. It extends medially and then downward midway between the inner canthus of the eye and the middle of the dorsum of the nose, then down the nasofacial sulcus to end just below the free edge of the nasal bones. The incision is carried through the soft tissues and periosteum and down to the bone. Continuous suction throughout the operation is employed and bleeding points are ligated or coagulated with the electro-surgical unit. By means of a sharp periosteum elevator the periosteum is elevated from the bone medially as far as the middle of the nose and laterally as far as the lacrimal bone care being exercised to avoid damage to the lacrimal sac. Elevation of the lacrimal sac from its fossa and of the periosteum from the lamina papyracea may be required if extension of the tumor into the ethmoid cells makes it necessary to explore the whole ethmoid region. An incision is made through the nasal mucous membrane along the lower free edge of the nasal bone and the mucous membrane is freed from its undersurface of this bone. Access to the nasal cavity is then gained by using a rongeur to remove portions of the nasal bone and of the nasal process of the maxillary and frontal bones, after which

an incision is made through the nasal mucous membrane parallel to the skin incision to expose the interior of the nasal cavity. The point of attachment and extent of the tumor then are determined. If the attachment is mainly in the ethmoid region it becomes necessary to expose the ethmoid cells by removal of the lacrimal bone and a portion of the lamina papyracea of the ethmoid bone. If the attachment is in the region of the maxillary ostium it usually is advisable to open the maxillary sinus as is done in the Caldwell-Luc operation and to examine this sinus carefully for extension of the tumor. Examination of the frontal or sphenoid sinuses may be necessary. After removal of the tumor the point of attachment is thoroughly electrocoagulated and radium is applied over the coagulated region. The radium is held in place with gauze packing so arranged that both the radium and packing can be removed through the nostril. The wound is then closed with subcutaneous interrupted catgut sutures and the skin edges are approximated with black silk. A pressure dressing is then applied. The sutures are removed in three or four days. The scar usually is quite inconspicuous.

MOUTH

Fig. F. A. and Rowland W. D. Primary Tumors of Stensen's and Wharton's Ducts. *Arch Otolaryngol.*, 1944, 40: 175

A tumor arising in Stensen's or in Wharton's duct is rare, but 2 cases of adenocarcinoma of the main salivary ducts have come under the observation of Figg and Rowland in recent years and in addition 2 inflammatory nodules occurring without salivary calculi have been encountered in these structures.

The symptoms complained of in the cases of true neoplasm were not uniform. In one case they were those characteristic of recurring obstruction of Stensen's duct, and in the other (the case of adenocarcinoma of Wharton's duct) the patient had noted two small, tender nodules in the right side of the floor of the mouth situated anteriorly along the course of the submaxillary salivary duct. These had increased steadily in size but had not produced evidence of obstruction to the flow of saliva.

The tumors were firm movable, slow growing nodules and each appeared to be encapsulated within the wall of the duct, so that they were relatively easy to remove. They were excised the duct being amputated and in one of the cases the proximal stump of the duct was inserted into a stab wound in the cheek posterior to the site of the original orifice. Interstitial radium therapy was given to the operative wounds.

The two distinct nodules present in the submaxillary salivary duct in the second case proved to be malignant.

NOAH D. FABRICANT, M.D.

Burger, R. E., and Lehman, E. P.: Leontiasis Ossea Complicated by Marjolin's Ulcer. *Surgery* 1944, 16: 542

The author states that this case of leontiasis ossea, originating in youth, seems to belong to Group I of Monti's classification. Although it adds nothing to our knowledge of the etiology of the disease, it presents several aspects of interest.

In the first place the spontaneous sloughing of the dense maxillary lesions with apparent local cure is unusual. This was presumably the result of infection similar to the process in the mandible for which the patient was first treated at this hospital. The



Fig. 1.



Fig. 2.



Fig. 3.

Fig. 1. Photograph of the patient in 1930, revealing the large lower jaw.
Figs. 2 and 3. Photographs taken November 1943 show

ing the regression in the visible epidermoid carcinoma and thenarked increase of puckering of the flap, possibly due to infiltrating tumor

arrest of the disease in this area may have protected him from the effects of craniostenosis. It raises the question as to whether radical excision of the diseased areas in an early stage might modify the gradual spread of the lesion. Coppo is stated to have reported a case of resection of the right superior maxilla for leontiasis ossea.

The present case is also interesting on account of the enormous size of the jaw lesion which in itself caused complete disability. One of the earlier cases shows a tumor of the jaw comparable to the present example. In the third place, the case illustrates the spread of the process into the upper cervical vertebrae a phenomenon reported previously. The limitation of the process to that portion of a bone arising in a simple anlage as described by Mayer is illustrated by the escape of the intermaxillary process although the superior maxilla on each side was involved to a marked degree.

Finally the complicating epidermoid carcinoma which determined the outcome of the case is unique. This neoplasm is unquestionably of the same nature as Marjolin's ulcer occurring in chronic ulcer of the skin and in chronic sinuses. The incidence of epidermoid carcinoma in a buccal fistula has not been made the object of a search of the literature but it must be very rare. JAMES C. BRASWELL, M.D.

PHARYNX

Szanto, P. B. and Hollender, A. R.: Tuberculosis of the Nasopharynx. *Ann. Otol. Rhinol.*, 1944, 53, 303.

Tuberculosis of the nasopharynx has been a neglected medical problem. As a complication of pulmonary tuberculosis its incidence is greater than that of tuberculosis of the larynx.

Among 134 consecutive autopsies in which a general pathological study of the nasopharynx was performed there were 24 subjects with various forms of pulmonary tuberculosis, and, of these, 18 (75 per cent) showed tuberculous involvement of the nasopharynx.

Histopathological study is often essential for a positive diagnosis of nasopharyngeal tuberculosis.

The nasopharynx may be the site of a persistent focus of tuberculous infection, and this may frequently explain the source of reinfection of the lungs in persons who have previously experienced an arrest of pulmonary involvement.

It is suggested that a plea is made for careful, routine clinical investigation of the nasopharynx in all rhinolaryngological examinations, especially in patients with pulmonary tuberculous disease. JOHN F. DILLER, M.D.

NECK

Shirer, J. W.: Modification of the King Operation for Bilateral Paralysis of the Vocal Cord. *Ann. Surg.* 1944, 20, 617.

Shirer states that his modification of the King operation is simple and provides a sufficient and

adequate airway for removal of the permanent tracheotomy tube. JAMES C. BRASWELL, M.D.

Clerf, L. H.: The Pre-epiglottic Space: Its Relation to Carcinoma of the Epiglottis. *J. A. Otolaryng. Chlc.*, 1944, 40: 177.

The pre-epiglottic space is described by anatomists as triangular or funnel-shaped in sagittal section, with the base directed upward. It is an actual space, filled with cellular and adipose tissue; it contains no lymph nodes but is traversed by lymphatic vessels. The anterior and anterolateral walls are formed by the upper portions of the wings of the thyroid cartilage and thyrohyoid membrane. This membrane is strengthened by elastic fibers in the midline and at all the tips of the greater cornua of the hyoid bone forming the median and lateral thyrohyoid ligaments. It is pierced on each side of the midline by the superior laryngeal vessels and the internal division of the superior laryngeal nerve, and it also transmits a few efferent lymphatic vessels. The base is closed by the hyoepiglottic aponeurosis or ligament which extends from the upper margin of the body of the hyoid bone to the anterior surface of approximately the middle of the epiglottis and corresponds to the bottom of the vallecula. The posterior boundary is formed by the epiglottis extending from the hyoepiglottic aponeurosis above to the thyroepiglottic ligament, which is situated immediately above the anterior commissure. Since the lower part of the epiglottis becomes narrowed, the remainder of the posterior boundary of the pre-epiglottic space is formed by an elastic membrane. This can, therefore, be considered as the weak wall of the pre-epiglottic space, as the epiglottis itself affords little protection against cancerous invasion consisting as it does of thin yellow elastic cartilage.

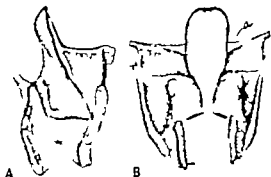


Fig. 1. A, Sagittal section of the larynx showing the pre-epiglottic space and its boundaries. The thyroid membrane and the thyroid cartilage are anterior. The hyoepiglottic aponeurosis above forms the base and the epiglottis and the thyroepiglottic ligament are posterior. B, Schematic drawing to show the defect or weak portion of the pre-epiglottic space, which is formed by the epiglottis from the level of the hyoepiglottic aponeurosis above to the thyroepiglottic ligament below. The lateral margins are closed by elastic membrane.

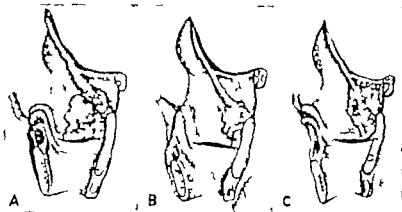


Fig. 2. A, Extensive cancer of the vestibule which extended a considerable distance along the left ventricular band, crossed the anterior commissure and involved the anterior end of the right ventricular band. The lower two-thirds of the posterior surface of the epiglottis also was involved. Invasion of the pre-epiglottic space was widespread but had not penetrated deeply. B, Cancer of the vestibule of the larynx which involved the extreme anterior ends of both ventricular bands. There were no disturbances of the voice. Although the epiglottic involvement was extensive, it could not be visualized by mirror laryngoscopy because of an overhanging epiglottis. Invasion of the pre-epiglottic space extended to the median thyrohyoid ligament. C, Extensive invasion of the pre-epiglottic space by a vestibular cancer which exhibited a relatively small surface lesion. Because of the close proximity of the invading mass to the hyoepiglottic aponeurosis, incision across the pre-epiglottic space would have resulted in incomplete removal of the cancer.

which exhibits many depressions even perforation and rarely undergoes ossification.

The anterior invasion of the pre-epiglottic space is important for it cannot be determined by mirror laryngoscopy or by direct examination. While much information can be secured with lateral roentgenograms of the larynx, these commonly exhibit only the more dense portions of the cancer. It is common to find cancer cells by microscopic examinations of the pre-epiglottic space well beyond the apparent anatomic margins of the growth. The thyrohyoid membrane and the hyoepiglottic aponeurosis offer marked resistance to neoplastic invasion so that in cases of pre-epiglottic invasion, involvement of the base of the tongue or penetration of the thyrohyoid membrane to the front of the neck is rare. There commonly is metastasis to the regional lymph nodes long before this occurs.

The lymphatic drainage from the base of the epiglottis and the anterior extremities of the ventricular bands is carried across the pre-epiglottic space through the thyrohyoid membrane to the upper nodes of the deep cervical group. Occasionally one or more vessels pass upward and terminate in a node situated below the posterior belly of the digastric muscle, but metastasis to this is uncommon. In 2

recent cases of carcinoma of the base of the epiglottis, Clerf discovered small nodes immediately above the hyoid bone on the mylohyoid muscle. These apparently were submental nodes which, usually arranged in transverse direction, occasionally may be placed vertically and then one is in close relation to the hyoid bone. In these 2 cases the position of the submental nodes apparently conformed to the latter arrangement. In neither of these was there any histological evidence of carcinoma. Since carcinoma of the anterior portion of the larynx above the vocal cords invariably perforates the epiglottis and commonly invades the pre-epiglottic space before it is recognized clinically it is necessary to deal surgically with this space. Invasion through the hyoepiglottic aponeurosis is rarely observed therefore a surgical approach which does not enter the pre-epiglottic space should be employed. If one removes the hyoid bone with the larynx by incision through the muscles above it and keeps the operation above the hyoepiglottic aponeurosis the incision always is through normal tissue. Laryngectomy with extirpation of the pre-epiglottic space, or pre-epiglottic laryngectomy would seem to be the rational surgical procedure to practice in all these cases.

J. M. MOXA, M.D.

SURGERY OF THE NERVOUS SYSTEM

PERIPHERAL NERVES

Harvey A. M., and Kuffler S. W.: Motor Nerve Function with Lesions of the Peripheral Nerves: A Quantitative Study. *Arch. New Psychiat. Chic.*, 1944, 52: 317

A simple test has been devised to determine the localization and extent of nerve injuries as well as to estimate quantitatively the recovery of function or the effect of treatment. This test consists of recording by means of electrodes—similar to the recording of encephalographic findings. The electrodes are carefully applied over the muscles to be tested and the leads are recorded through a connection with an electrocardiograph or an electroencephalograph. Nerve stimulation is produced at a higher level by breaking the current flow in the primary of an induction coil with a Morse key (or any suitable type of contact breaker). Two stimulating electrodes lead from the secondary coil to the patient, one "indifferent" which consists of a large copperizing plate in contact with the patient's extremity 10 or 20 cm. above the point along the nerve to be stimulated. The second stimulating electrode consists of a small round metal disc attached to the end of a hardwood rod covered by gauze and lint. The arm must be held as quietly as possible during the recording. Stimulation of the nerve for consideration is accomplished at a suitable point where it is most accessible. The maximal motor nerve stimulus is applied by the stimulating electrode and the action potential is then recorded from the recording electrode leads to the recording device. A group of normal action potentials for various muscles resulting from maximum motor nerve stimulus, has been recorded. A comparison with these figures, more particularly with those of the opposite sides of the body, allows one to estimate the degree of nerve function present.

This test has been advocated for differentiation between organic and hysterical paralysis, as well as for estimates of recovery following peripheral-nerve disease or injury. **HOWARD A. BROWN, M.D.**

Harvey A. M.: A Type of Neuritis Associated with Malarial Fever. *Bull. J. Neurol. Hosp.* 1944, 75: 225.

A study of a group of malarial patients with various neurological manifestations or involvements of the nervous system is presented in this report by the author. The symptoms were very protean in character and in the milder cases were largely subjective in nature.

The subjective sensory manifestations consisted of "numbness" drawing sensations in the muscles and the feeling of an extremity going to sleep. These were often bilateral and of very short duration, appearing after exercise or at night

awakening the patient from sleep. More severe subsequent attacks were associated with detectable neurological signs, such as hyperalgesia, hypalgesia, or hypesthesia. The areas involved were varied—peripheral radicular or glove type in distribution.

Signs of motor disturbances were noted during the subjective complaints of "drawing" sensations and comprised either involuntary fascicular movements or gross contractions of the flexors of the forearms and fingers as well as occasional involvement of the lower extremities. These manifestations, which persisted for several days to weeks were all accompanied by hyperalgesia.

Sympathetic autonomic irritation was manifested by cold blotchy cyanotic, hyperhidrotic areas in the site of the neural involvement. This occurred only in the more severely affected cases.

It is of interest that although the majority of these cases occurred during the first or second attack (including the period immediately following the attack) organic signs of neural involvement were more pronounced during subsequent attacks. The data given do not correlate the amount or period of medication; however it is understood that all of the patients were under medication at the time that they developed their neurological signs.

The author endorses Anderson's pathological findings that a vascular basis is the cause of the damage to the nervous system since the symptoms are best accounted for by this explanation.

JACK WOOD, M.D.

BRAIN AND ITS COVERINGS CRANIAL NERVES

Roos, W. D., and McNaughton, F. L.: Head Injury: A Study of Patients with Chronic Post-traumatic Complaints. *Arch. New Psychiat. Chic.* 1944, 52: 255

The cause of post-traumatic complaints or syndromes has passed through many phases of terminology and theorization. The authors present an evaluation derived from a careful study of 93 head injury subjects by physiological, psychological, and neurosurgical means.

The severity of the injury was rated according to post-traumatic amnesia, the number of red cross of the spinal fluid x-ray evidence of damage to the skull and abnormal findings on neurological examination. Both the electroencephalographic and pneumoencephalographic studies rated by Jaxer and Child respectively were found to show a fair correlation with the degree of injury. After a period of approximately two years the electroencephalographic abnormalities regressed while the pneumoencephalographic abnormalities persisted.

The personality of each patient was carefully evaluated by planned psychiatric interviews. Six

nal factors were tabulated according to type and their relation with the injury. Various psychological tests were used. The Shipley-Hartford test showed relation to the severity of injury. The Kraepelin continuous subtraction test and repetition of digits were of no definite help in this study. Striking results, however, were obtained by the Rorschach test differentiating the psychogenic from the cerebral organic disturbances. Repeated testing revealed a continuous flux which varied with the improvement of the condition. By means of the Rorschach method and psychological or personality factors the patients were classified and rated according to the degree of disability or instability revealed in each case.

Headaches have been one of the most common complaints of the patients after head injury; these are divided into several types. The localized and migrainous variety were more frequently associated with organic disturbances while the generalized and tense headaches were associated with psychological factors. Patients with localized headaches were found to be in better condition than those in other groups. The Rorschach test revealed a low instability and high disability rating which corresponded with the evidence of organic disturbances in electroencephalographic and pneumoencephalographic tests. It was of interest to note that even this group of patients were influenced by personal situational factors.

A re-evaluation of the subdural and spinal insufflation treatments was suggested by Penfield, who first used these procedures. It was found, however, that the long term results were no better than the results following pneumoencephalograms, and that for some of these patients could the influence of other factors be ruled out. The results in a few patients treated by a direct operative procedure suggest a limited application of such measures in carefully selected cases. The use of prostigmine was also of value. Its effect upon postural vascular responses is shown by slowing of the pulse rate, but there was no alteration of the headache.

The main concept carried throughout this study is that there is no specific syndrome following head injuries and that in all both organic and psychogenic factors as well as their admixture, must be evaluated for the individual patient.

JACK WOOLF, M.D.

Sarburg O. and Casamajor L. Phlebotomias and Phlebothrombosis of the Brain in the Newborn and in Early Childhood. *Arch. Nerv. Psychiat.* Chic., 1944 53: 170.

The basis of this report is a rather rare condition and a controversial one. It has to do with cyst formation and softening of the brain in children shortly after birth or before birth and results in the clinical picture of dementia, spasticity and finally death. The authors wish to show that the condition is primarily due to obstruction and thrombosis in certain of the venous areas of the brain and that this con-



Fig. 1. Final state of the process.

dition results from trauma before or during birth. There is a clinical discussion of some of the literature especially the German literature on this subject, and 2 illustrative cases of their own.

The first case was that of a child seen when he was nine months old. He had been normally delivered but from birth had not been active, had not eaten well and had not taken any interest in his surroundings. At the age of four months convulsions had set in with opisthotonos. The child died at the age of nine months. The brain was then examined and it forms a basis for this discussion.

The second case was that of a child who reached the age of thirteen years before he died. He was normally delivered but when he was two and one half months old it was noted that he did not move his leg and that he had a curvature of the spine. He could not sit up nor hold up his head. Pneumonia developed when he was eighteen months old. This child was first seen in the Neurological Institute when he was about two years old. At that time he showed marked spasticity and primary optic atrophy. The condition became more and more marked until finally a stage was reached which is illustrated in the accompanying figures.

This child constitutes the second case on which the argument is based. The pathological changes in the brain were necrosis in the centrum semiovale of the brain with softening which was followed by total or partial destruction of the brain tissue and resultant cyst formation. The least resistant structures that is the myelin sheaths and the axons were first destroyed and the more resistant structures, the glia were spared until very late in the condition. In the stages of complete destruction cyst formation occurred and in incomplete destruction sclerosis. The site of the lesions corresponded to the drainage area of certain veins notably the vena cerebri magna of Galen and the area drained by the superior sagittal sinus.

The clinical picture was as follows

The children were apparently normally delivered but after a few weeks they showed signs of a disease

which ended in an excessive increase in muscular tone opisthotonos flexed arms stretched legs, clenched fists talipes equinovarus, and exaggerated reflexes. In the pathological studies of the complaint the authors were able to show evidence of venous obstruction by stasis and venous obstruction by thrombosis in the areas of drainage of the veins already described. They are quite unable however to be sure that infection did not play an important role. The condition is, apparently, analogous to swayback in lambs. The article has some very good illustrations and the argument is quite extensive and as was mentioned before it introduces many similar cases from the literature.

LORREN VERBURGH, M.D.

Raaf, J., and Kernohan, J. W.: The Relation of Abnormal Collections of Cells in the Posterior Medullary Velum of the Cerebellum to the Origin of Medulloblastoma. *Arch. Neurol. Psychiat.*, Chic. 1944 53: 163.

The germinal bud from which the external granular layer of the cerebellum arises is situated at the posterior tip of the posterior medullary velum. It normally disappears before the end of the first month of extrauterine life. One hundred sixty-one fetal and infant cerebellums were studied, and abnormal collections of cells were found only in the region of the posterior medullary velum. Of 104 cerebellums in which the posterior medullary velum was examined microscopically, 23 were found to contain abnormal collections of cells. These cells were morphologically similar to the cells of medulloblastomas. In 8 of 25 cases of medulloblastoma the site of origin was found to be the posterior medullary velum; in the other 17 cases the site of origin could not definitely be established but it also may have been the posterior medullary velum. Since the site of abnormal collections of cells and the site of origin of medulloblastomas were found in the region formerly occupied by the germinal bud, the authors think that medulloblastomas originate frequently, if not exclusively, from cell rests which occur in the region originally occupied by the germinal bud.

Meads, M., Harris, W., Samper, B. A., and Finland M.: The Treatment of Meningococcal Meningitis with Penicillin. *England J. M.* 1944 3: 509.

Because of the good results obtained with sulfonamides there have been few reports of cases of meningococcal infection treated with penicillin. The gonococcus has been studied but the studies have been mostly confined to the treatment of sulfonamide resistant gonorrhea, which almost invariably responds to penicillin in adequate doses.

This study concerns 9 cases of meningococcal meningitis admitted to the Boston City Hospital, Boston, Massachusetts, during April, 1944. The ages of the patients ranged between fourteen and fifty-eight years. Some patients were acutely ill and irrational; 1 was acutely ill and rational and 1 was

only moderately ill when first seen. The duration of the acute illness before entry ranged from one to seven days and averaged about three days. Sulfonamide determinations of the blood were made routinely on admission in order to ascertain whether previous therapy by these drugs had been undertaken. No sulfonamide was found except in the last case. Lumbar punctures were done on admission and at intervals of from twelve to twenty-four hours. Cell counts, smears and cultures of the sediment, and chemical studies of the cerebrospinal fluid were carried out routinely. Blood and throat cultures were made on admission and in some cases were repeated once or twice daily until they were negative. Cultures and smears of the spinal fluid sediment were checked from time to time. With regard to treatment, all of the cases were started on penicillin, given both intramuscularly and intraspinally immediately after the diagnosis was made. The initial spinal dose consisted of from 10,000 to 20,000 units in 10 cc. of sterile physiological saline solution to replace a similar or larger volume of spinal fluid withdrawn.

From 5,000 to 15,000 units of penicillin were then given intraspinally at twelve-hour intervals for 2 or 5 doses, and every twenty-four hours after improvement was noted bacteriologically and clinically and this dosage was continued until clinical and bacteriological recovery took place. Intramuscular therapy consisted of doses of 15,000 units every three hours in 7 cases and of doses of 10,000 units every three hours in 2 cases. The total amount of penicillin given intrathecally varied from 30,000 to 150,000 units and averaged about 75,000 units. The amount of penicillin given intramuscularly ranged from 100,000 to 1,155,000 units and averaged about 500,000 units. Very careful records were kept of the patient and there is a large table summarizing each case with dosage, bacteriological effects, and results. In 1 case a convulsion occurred eight hours after the first lumbar puncture with the introduction of penicillin. In 6 cases improvement was first observed in from one to five days after the treatment was started (the average was about three days). In 3 cases there was a clinical recurrence, 1 on the 1st day and 1 on the fourth day. In these cases penicillin therapy was discontinued and sulfonylurea therapy was substituted for it. In the case in which sulfonamide had been given before admission the patient responded rapidly after twenty-four hours of penicillin treatment. Six patients became afebrile in from five to fifteen days, the average being almost ten days. In 3 cases the response was fast. In the first of these 3 the patient was afebrile in three and one-half days; in the second, after twenty-four hours; and in the third after fifty-two hours.

The conclusion was reached from the clinical and laboratory findings in these 9 cases of meningococcal meningitis treated with calcium penicillin, that sulfonamides are the drugs of choice in the treatment of group 1 meningococcus meningitis and that penicillin may be effective in group 2 meningococcus

meningitis in the doses used but the response is less favorable than that from sulfonamide therapy. Clinical response to penicillin is slower than that to the sulfonamides. Abnormal spinal-fluid chemical and bacteriological findings persist longer there may be recurrences and finally sulfonamides may have to be resorted to to effect a cure. Calcium penicillin is very effective against group 1 meningococcus bacteremia.

ADRIEN VERBRUGHEM M.D.

MISCELLANEOUS

Smith, A. DeF. Deery E. M., and Hagman, G. L.: Herniation of the Nucleus Pulposus. A Study of 100 Cases Treated by Operation. *J Bone Surg* 1944, 26: 821.

This study is based on 100 consecutive patients with herniation of a nucleus pulposus who were operated upon at the New York Orthopaedic Dispensary and Hospital, New York, between January 1937 and April, 1943. Low back pain to some degree was present in all but 1 patient. The results of the treatment are estimated in only 70 cases because the remainder of the cases were operated on less than one year before this report. It is the opinion of the authors that in many cases of herniation of a disc there is a deranged or unstable lumbosacral joint. They consider this important from many points of view. They believe, first that probably more fusions should be done than are being done and second that the problem is one which concerns not only the orthopedic surgeon but the neurological surgeon, and third that the best results will be obtained by co-operation between the two men.

Fusion was done by the Hibbs method in 83 cases. The indications for fusion were an unstable joint as determined by the roentgenograms with or without symptoms of back pain. The Hibbs method of fusion was employed because of the simplicity of combining it with interlaminar removal of the herniated disc.

With regard to the symptoms and physical signs there was a history of low back pain of varying duration in almost every case. The shortest history of sciatic pain was one month (2 cases) and the longest was ten years (4 cases) the others varied between these extremes. The sciatic pain was increased with coughing and sneezing in 55 cases but the results were not always recorded. There was a decreased or obliterated lumbar lordosis in 61 per cent. Raising of the straight leg was limited in only 70 per cent of the patients. The ankle jerk was definitely diminished or entirely absent in 85 cases. It was believed that the sensory changes were by far the most accurate means of discovering the site at which the herniation was to be found as neither the motor signs nor the narrowed intervertebral space, if there was one that could be seen on the roentgenograms could be relied upon to indicate the exact level of the herniation.

Air studies lipiodol studies and other similar tests are no longer used. Criteria for determining an unstable or mechanically deranged lumbosacral

joint, as seen in the roentgenograms, were numerous and included asymmetrical lateral articulations anterior or posterior displacement of the fifth lumbar body exaggeration of the lumbosacral angle a thin intervertebral disc, and a transitional or partially sacralized lumbosacral vertebra. With regard to the operation, the usual technique was employed with the exception that the patient was placed in a kneeling position with the hips flexed at 90 degrees. This was considered to be an important point in the technique of the operative procedure, especially if a fusion was to be performed. The patient was allowed up in a Taylor brace at the end of six weeks, and normal activities were usually begun about five months after the operation. Among the 83 patients who had a spinal fusion, failure occurred in 8 or about 12 per cent. However in 2 or 3 of these a good result was obtained by a secondary repair operation.

The results were classified as excellent good or poor. An excellent result was considered to have been obtained when the patient was able to return to the same occupation or one equivalent to that which he had before operation. A good result was considered to have taken place when only slight pain was felt and there was no disability. In the patients who had sufficient pain to cause partial or complete disability the result was described as poor. On this basis there were 24 excellent results 33 good and 13 poor.

ADRIEN VERBRUGHEM M.D.

Woodhall, B.: Fibrin Foam as a Hemostatic Agent in Rehabilitation Neurosurgery. *J Am. M. Ass.*, 1944, 126: 469.

Since the introduction of fibrin foam as a hemostatic agent by Ingraham and Bailey in 1944 this substance has been the subject of many examinations and its use is now past the experimental stage. It was made available to the Neurosurgical Section of the Walter Reed General Hospital, Washington D C. in the fall of 1943 and since January 1944 it has been used in a total number of 226 neurosurgical operations.

Hitherto control of hemorrhage in neurosurgery was confined to the use of silver clips the electro-surgical unit, hot cotton pledgets, and muscle clips. There are certain situations in which silver clips and the cautery cannot be used hot moist surgical patties are often ineffectual and time-consuming and muscle pledgets are by no means universally successful and often promote considerable tissue reaction. Fibrin foam on the other hand is useful in many situations and is a prompt hemostatic agent is absorbable and causes very little, if any tissue reaction. It is prepared from human fibrinogen and human thrombin and is kept in a dry state in which it appears dull white and brittle. A fairly large mass of fibrin foam is packaged sterile in a dry state and with a vial of dried human thrombin. A third vial contains 30 cc. of sterile isotonic solution of sodium chloride. At the operating table the thrombin is dissolved in the saline solution by means of vigorous

stirring. Fragments of fibrin foam are then dipped into the thrombin solution and removed and used as indicated. Pieces can be cut in accordance with the size that is desired. A piece of foam dipped in thrombin solution is removed and placed against the vessels that are bleeding and a moist cotton pledget is held against this until bleeding is arrested. This method is useful especially for venous hemorrhage and in oozing from vessels in the brain. It is not considered practical for arterial bleeding.

At the Walter Reed Hospital various types of cases were used to find out the value of fibrin foam. There were 102 cases of ruptured intervertebral discs, 86 of peripheral nerve injury, 23 of tantalum plating, 1 skull defect, 9 craniotomies for brain tumors, 5 laminectomies, and 1 acute cerebral laceration. The extradural bleeding which so often accompanies the removal of the herniated nucleus pulposus was quickly and easily controlled by means of fibrin foam. It is well known that in treatment of peripheral nerve injuries a small vessel on the perineurium may be torn and this is a situation in which neither clipping nor the electrocautery is useful. However, a small piece of fibrin foam when held against the bleeding vessel quickly stops it, and makes it possible to obtain an anastomosis of the nerve in a completely dry field. In another situation when cortical scars are being removed there is often left behind a shallow crater in which there is oozing from small blood vessels. In this case as in the other cases the

fibrin foam is placed in contact with the bleeding vessels, in the manner described, and is left in place. Fibrin foam has been found particularly useful in controlling the bleeding from the side of the pons and may accompany the complete removal of an acoustic tumor. In 1 instance the fibrin foam was used in an acute cerebral laceration caused by an explosion while the patient was welding a 50-gallon steel drum. After the small vessels of the acute cortical laceration were clipped and/or cauterized with the electrocautery there was still diffuse hemorrhage in spite of warm saline packs. This bleeding was instantly controlled by round discs of fibrin foam. Although this was an isolated experience, it appeared that fibrin foam might be of use in acute cerebral lacerations. During this time of war this information may be of considerable significance.

In all of the procedures in which the hemostatic agent was employed, the hemorrhage was controlled instantly. No clinical untoward reactions that could be attributed to the use of the fibrin foam were observed. On 2 occasions in which the wounds were re-explored an opportunity was afforded to observe possible tissue reactions from the fibrin foam, but in neither case was there any evidence that this method of hemostasis had caused any such reaction. It appears that this method of hemostasis promises a very good result for the future in war injuries involving the nervous system.

ADRIAN VERBULOGHEN, M.D.

SURGERY OF THE THORAX

TRACHEA, LUNGS, AND PLEURA

Alexander J: Roles of Medicine and Surgery in the Management of Bronchiectasis. *Ann. Int. M.* 1944, 21 565

From the point of view of treatment it is important that a distinction be made between (1) cases of bronchiectasis in which there is no obstruction of the larger bronchi (2) cases in which varying degrees of obstruction of the larger bronchi exist because of a foreign body bronchial carcinoma or adenoma, tuberculous granulation tissue or fibrous stricture in the bronchial wall, or pyogenic granulation tissue and extrabronchial pressure by enlarged lymph nodes or other tumors and (3) those relatively infrequent cases which present the characteristic symptoms of bronchiectasis but in which no bronchiectasis exists, the symptoms being due to allergic or asthmatic bronchitis or true chronic catarrhal bronchitis. The presence or absence of bronchiectasis can be determined accurately only by good bronchograms, whereas differentiation between the first and second groups mentioned in this paragraph can best be made by bronchoscopy. Although bronchograms frequently reveal even partial bronchial obstruction they do not reveal its nature.

Lobectomy is without question the treatment of choice for those patients (1) whose age, cardiorespiratory functional reserve and general condition are suitable (2) whose lesions are restricted to one lobe to the right lower and middle lobes to the left lower and lingular (left middle) lobes or in some cases to all the lobes of one lung (total pneumonectomy) to one lobe of each lung or to two lobes of one lung and one lobe of the other lung (bilateral lobectomy) and (3) who have failed to attain a satisfactorily stable condition of improvement from nonsurgical treatment. Special additional reasons for performing lobectomy in childhood are that the dangers of bronchiectasis are particularly great then and that the removal of the lesions makes probable a normally long life of health in place of a probably short life with varying degrees of illness and disability. The indications for lobectomy may become further extended in certain cases of multiple lobe bronchiectasis by the wider application of Churchill and Bellamy's suggestion that in certain cases only the affected segments of the lobes be removed. This principle has been applied for a number of years in the removal of the lingular segments of the left upper lobe, which is technically simpler and safer here than in any other lobar segment.

The present safety of pulmonary lobectomy has solved the problem of treatment for approximately half the patients with bronchiectasis but the other half are for various reasons (especially because of extensive bilateral lesions) not suitable for the operation. Nonsurgical methods of treatment, if properly

and faithfully carried out, can be made effective in greatly alleviating the distressing symptoms of the disease in a large majority of patients in spite of the pessimistic opinions about the value of nonsurgical treatment that have recently been expressed by a number of physicians.

Postural drainage is the most valuable of the non-surgical therapeutic measures. A bronchoscopy carried out immediately after a postural drainage determines the relative number of retained secretions and therefore gives an indication of the probable effectiveness of postural drainage.

Every bronchiectatic patient should have at least one bronchoscopic examination not only because some otherwise undetectable, important intrabronchial lesion may be discovered, but also because the aspiration of secretions and the chemical shrinkage of the bronchial mucosa often bring about improvement in the symptoms which in occasional cases (notably in children, but also in adults) is astonishingly great. Bronchoscopy is also of great value in preventing the development of bronchiectasis in early cases of pneumonitis or 'unresolved pneumonia'. An effective treatment, which should be immediately preceded by a postural drainage and which may occupy from fifteen to thirty minutes requires (1) that the bronchi containing secretions should be repeatedly aspirated until all free secretions have been removed (this is to be done both before and after the mucosa has been shrunken and the patient has repeatedly coughed on command) and (2) that equal parts of a 2 per cent pontocaline hydrochloride and 1 to 2,000 epinephrine solutions or other shrinkage drugs, be directly applied, step by step to all parts of the mucosa that are swollen, and that an excess of the solution in the gauze pledgets be squeezed into those bronchi of the affected parts of the lung that are too small to be directly reached by the pledgets or a small amount of the solution be injected into these bronchi.

Since the primary purpose of nonsurgical treatment is to bring about the maximal evacuation of secretion cough medicines that check the cough reflex are not helpful but harmful and measures that promote expectoration are beneficial. Such expectorants as ammonium chloride, iodides, ipecac steam inhalations, which may be medicated with benzoin or menthol and the inhalation of a nebulized spray of 1 to 100 dilution of epinephrine solution may prove useful if the secretions are thick and especially viscid and if expectoration is difficult.

Only in exceptional cases has chemotherapy proved useful. Intravenous arsenicals which are especially dangerous in patients having a prolonged suppurative disease, have occasionally reduced pulmonary infection when it was caused chiefly by the Vincent group of organisms. The sulfonamides whether given by mouth or by a nebulizer have been

disappointing in chronic bronchiectasis although an excellent effect has been produced in a few patients.

Treatment of infection in the nasal sinuses, nose, mouth, and pharynx should be given and may improve the bronchiectasis symptoms.

General hygienic measures are indicated in most cases of bronchiectasis. Ideally patients who have even mild fever and who are fatigued and under weight should be put to bed for a period of weeks or months under the sanatorium type of regimen, or should at least spend long hours in bed at night and two hours in bed after lunch. Generalized heliotherapy may be helpful as a hygienic measure, but should not be used in febrile patients or in those subject to recurrent attacks of pneumonitis. Anemia should be treated by blood transfusions if necessary.

The author found allergic desensitization disappointing.

In certain cases of bronchiectasis with repeated severe hemoptyses temporary phrenic paralysis may stop the bleeding, but this operation should not be used if the patient has difficulty in raising his bronchopulmonary secretions.

The author is opposed to induced pneumothorax, roentgen-ray therapy "the thirst cure," and the many operations that have been proposed, or used with poor results, before the operation of lobectomy was developed to its present status of safety and effectiveness.

JOSEPH K. NARAT, M.D.

Shank, P. J.: Empyema of the Lung, A Review of the Literature and an Analysis of 169 Cases. *Am. J. Surg.* 1944, 66: 224.

Empyema per se is rarely if ever a primary disease. It is most frequently secondary to pneumonia, influenza, or measles. Approximately 75 per cent of all empyema is due to the pneumococcus and 15 per cent to the streptococcus, the remaining 10 per cent is due to staphylococcus, influenza, and other rarer types of organisms.

The diagnosis of empyema depends upon a septic temperature, flatness on percussion, roentgenographic findings and the aspiration of pus from the chest. It is important that diagnosis be made early. Treatment consisting of thorough and rapid evacuation of the pus should be instituted, to spare the patient prolonged infection and complications. Frequent and early roentgenograms will produce many more early diagnoses. Roentgenograms should be made in the oblique as well as the frontal and lateral planes, as many interlobular encysted, and pulmonary abscesses may be demonstrated. Of all the diagnostic procedures, aspiration remains the definite means of diagnosis after accurate localization of the pus by the roentgenograms. The aspiration of tuberculous pus may lead to disastrous results if the condition is treated by open or closed thoracotomy. Aspiration is also important in determining the proper drainage site. In location, empyema is usually found in one of the lower lobes, but it may be multifoliated. Recognition of multiple loculation depends upon careful study of posteroanterior

lateral and oblique roentgenograms. The loci should be drained as they are recognized, either through the original or supplementary incisions.

In any treatment of pleural empyema, the objectives to be attained are the nutrition of the patient, as complete and early drainage as possible, and expansion of the lung. To be excluded are: operative shock, mediastinal flutter and chronicity. Elker and Graham have stated that the first aim should be to save lives. Secondary to this are: (1) complete evacuation of the pus (2) rapid elimination of toxicity and systemic effects (3) sterilization and subsequent complete closure of the cavity with obliteration of all foci of infection (4) complete healing of the external wound (5) restoration of the patient to his normal social and economic position (6) avoidance of chronic empyema and recurrences and (7) accomplishment of these results in as short a time as possible.

Aspiration should be used in all cases at the beginning of treatment and should be repeated before operation, to relieve mechanical embarrassment due to the accumulation of fluid in the pleural cavity and to alleviate the toxic symptoms during the synpneumonic stage. Multiple therapeutic aspirations should be done in encysted empyema and followed by the injection of air in order to outline the cavity in the roentgenogram. While the diagnosis of thoracic empyema should never be made without the introduction of a needle and the removal of pus, the treatment of empyema by multiple aspirations should not be continued after four or five aspirations unless the patient shows a marked response to the treatment.

Intercostal closed drainage is advised particularly when reamobilization of fluid after aspiration is so rapid that even daily aspirations fail to give adequate relief. Closed operations are those in which a catheter is inserted into an empyema cavity through an intercostal space without exposure of the parietal pleura. It is believed that no form of closed drainage stays absolutely airtight for more than a week or two. Airtight drainage for more than two or three weeks is rarely necessary. It should not be continued longer than this unless there is improvement shown by the clinical condition with a decrease in the size of the cavity and re-expansion of the involved lung. If a week or two of intercostal closed drainage does not prove adequate, especially in the pneumococcal type of infection, the patient's condition should be improved sufficiently to warrant open surgical drainage.

In properly selected cases, open drainage is one of the most efficient methods of treating empyema, since it allows exploration of the pleural cavity for the identification of bronchial fistulas and possibly accessory empyema pockets, and permits complete removal of all fibrin masses and the proper placement of the tube.

Patients with thoracic empyema, having a reduced vital capacity are in a state of air hunger a greater part of the time, hence the anesthetic that gives the

least pulmonary embarrassment should be selected. It must (1) avoid reducing the vital capacity below the level to which the patient has become accustomed during his illness. (2) allow the lateral position of the patient on the operating table on his sound side. (3) prevent loss of blood as the thoracic wall is a very vascular bed and (4) deal with the copious amount of sputum. Diagnostic and therapeutic aspirations can all be performed following the local infiltration of novocaine or of one of its derivatives. Rib resections can be done under local anesthesia but some patients object to the cutting of the rib and a general anesthetic must be given. Ethylene is a good general anesthetic and seems to meet all requirements. It has the added advantage of allowing a higher intake of oxygen. Cyclopropane maintains the highest percentage of oxygen in the circulating blood which factor is so important in patients with a reduced vital capacity. Unfortunately in a certain percentage of patients who have cardiac lesions, cyclopropane is contraindicated and may prove fatal by producing ventricular fibrillation. Positive-pressure anesthesia should be used when the pleural cavity is opened. Endotracheal anesthesia and suction must be employed in the presence of copious amounts of sputum.

The postoperative treatment of thoracic empyema, particularly in children is of paramount importance, for on it depends the rapid and complete recovery of the patient. Adherence to minute details is mandatory to prevent too early closure of the cavity and a resultant chronic infection. Physical examination of the chest is of little value. Frequent estimations of the capacity of the cavity along with frequent roentgenograms are the only accurate method of determining progress of the disease. Following the evacuation of the pus and the receding in size of the empyema cavity the re-expansion of the lung is followed closely. Blow bottles have long been used to aid and increase the speed of re-expansion of the lung and of reduction in size of the cavity. It is difficult even now to make any final remarks on the efficiency of the sulfonamide drugs in the treatment of pneumonia, since there are so many variable factors in its treatment. A few facts of significance have emerged namely sulfanilamide does not produce any dramatic change in the course of hemolytic streptococcal pneumonia and it does not seem to reduce the incidence of empyema. Lastly but most important in the postoperative care, is maintenance of the patient's nutrition. He should receive a well balanced high caloric, high vitamin diet. The loss of plasma proteins from the large, raw necrotic area of the pleural abscess cavity may be compared to the loss of plasma proteins from a burn of like size and must be replaced by transfusions of plasma as well as of whole blood.

Empyema complications result in most instances from long delayed treatment. If not drained surgically the pus may burrow in many directions and cause perforation into a bronchus or empyema necessitatis or perforation into the trachea, esophagus,

pericardium blood vessels, or mediastinum. Occasionally it may penetrate the diaphragm to the peritoneal cavity or to the extraperitoneal region. Transdiaphragmatic and retrodiaphragmatic extension of infections may occur. Infections of the chest wall are not regarded as serious complications and are rather infrequent. Scoliosis is a complication of empyema which varies directly with the duration of the empyema and inversely with the patient's age.

A proper understanding of the pathology and pathological physiology of acute empyema and its application to the treatment of the disease would render chronic nontuberculous empyema a clinical rarity. If there is evidence of a considerable cavity four or five weeks after drainage of the purulent exudate and if the tissues are not well healed about the tube it is well to do a secondary rib resection and remove the rib above or below the original drainage. This also holds true for any secondary abscess draining into the main empyema cavity. Hindrance of the free outflow of the discharge in a secondary cavity results in more invasion of the wall and more protective response from the surrounding tissue. Chronic empyema implies attenuated infection such as might readily occur with an intermittent discharge slightly slower than the accumulation or with an undrained discharge. The essential cause is granulation tissue which replaces the pleura under repeated infection. Another cause fortunately not common is the presence of foreign bodies in the pleural cavity. In the treatment of chronic empyema the more conservative method should be given a fair trial before more mutilating ones are attempted. Carter lists the three classes of chronic empyema requiring surgery as follows: (1) secondary tuberculous empyema, (2) pyogenic empyema of several years duration and (3) chronic empyema with bronchial fistula. Three unroofing operations of short duration are preferable to one prolonged one. Empyema cavities decrease remarkably in size from one stage to the next so that the ultimate amount of rib removal is less for the operation in stages.

Putrid empyema is a pathological entity deserving separate consideration. Effective treatment depends upon thorough knowledge of its pathogenesis, pathology and clinical manifestations. The contents of a putrid empyema abscess cavity consist of foul pus and detritus gathered in one or more compartments. Following disclosure of foul pus or foul air operation should be performed immediately since nothing can be gained by delay and after the aspiration of foul pus there is a possibility of the development of putrid phlegmon in the chest wall. This usually dissects between the ribs and intercostal muscles and may not be recognized for several days. Immediate improvement is seen after evacuation, ventilation and aeration of an anaerobic infection. Wide unroofing allowing full visualization of the cavity is imperative in order that drainage may be maintained to the bronchial fistula and for better drainage of the pulmonary abscess. Rib resection should be just short of the limits of the lesion to prevent entry

into the uninvolved portion of the pleural space. The cavity and all its recesses are then packed with iodoform gauze or zinc peroxide. Closed drainage is justified in putrid empyema only because of the danger of open operation when the mediastinum is mobile. A basic objection to closed drainage is its inability to eradicate the anaerobic infection without free ventilation. The mortality rate need not be high if there are early recognition, accurate diagnosis and immediate treatment. Immediate open drainage gives the best results. All less radical methods give unreasonably high mortality rates.

The results in these 169 cases of nontuberculous thoracic empyema with 11 deaths are quite comparable to those in other recently reported series. The mortality rate of 6.5 per cent is recorded. The cases have been divided into two groups for study, one group comprises those patients twelve years of age and under and the second group those over twelve years of age. The cases have been studied in three five year series. There is very little difference in the mortality rate for these periods except in the last five year period when the mortality rate for putrid empyema increased to 40 per cent. One hundred and five males and 64 females had thoracic empyema. There were 83 cases with involvement on the right side and 83 with involvement on the left side. Four patients had both sides involved. The pneumococcus which was the most frequent organism found, was responsible for 73 per cent of the cases of thoracic empyema, the streptococcus for 20 per cent and the staphylococcus for 3 per cent. The other types of organisms were responsible for the remaining cases of empyema. There were 9 cases of putrid empyema. Otitis media was the most frequent complication and associated condition. Treatment consisted of various operative procedures. Aspiration with subsequent rib resection and open drainage was carried out 91 times. Thirty-seven patients were subjected to aspiration and closed intercostal drainage followed by open rib resection. Sulfonamide therapy was used on some patients mostly by the family physician before they arrived at the hospital and it is difficult to evaluate the results. It has a beneficial effect in lowering the mortality rate, but it has not appreciably altered the development of empyema. CHARLES BARON, M.D.

HEART AND PERICARDIUM

Neuhof, H.: Indications for Pericardiectomy with Special Reference to the Exposure of an Infected Patent Ductus. *J. Thorac. Surg.* 944, 3 374.

In addition to the four standard indications for pericardiectomy with or without drainage, (hemopericardium, suppurative and constrictive pericarditis, foreign bodies, and neoplasms) seven further conditions in the author's experience are described with illustrative case histories, in the hope that other surgeons will join in broadening the indications for the procedure.

The first condition was that of neoplastic disease of the left lung, in which extensive adhesions to the parietes posteriorly rendered informative palpation of the posterior aspect of the hilus impossible. Pericardiectomy with palpation within revealed involvement of the nodes at the hilus and the inoperable character of the lesion.

In another case a pericardiectomy was performed to relieve the cardiac tamponade effect of a serous pericardial effusion during anesthesia in operation for tumor of the left lung. Exploration within the pericardial sac itself disclosed the inoperable character of the lesion.

A third patient was operated upon for a pulmonary neoplasm. The lesion appeared at first to be inoperable because of fixation at the mediastinum and invasion of the pericardium, but exploratory pericardiectomy revealed the extent of the invasion. Liberal sacrifice of the pericardium made possible an adequate excision of the tumor. In order to cover the large pericardial defect, the pulmonary tissue adjacent to the stump was approximated to the mediastinal tissues medial to and above the pericardial defect.

A fourth instance was that of a twenty-three-year-old man, with a history of abdominal distention for three months. On admission his abdomen was tense with fluid and the blood pressure was 116/96, the venous pressure 19 cm. At operation the pericardium was apparently not thickened but it was somewhat opaque (restrictive pericarditis). Cardiac pulsations were normal. When the pericardium was incised it was found to be very slightly thickened. The lesion was an adhesive fibrous one of the visceral pericardium. Visceral membrane was generously removed. The freedom from aortic subaortitis (four years since operation) seems to suggest pericardiectomy in such cases, even in the presence of a pericardial sac which appears to be normal externally.

Another instance in which pericardiectomy seems indicated is when a patient does react well following initial pericardiectomy for the drainage of a suppurative pericarditis in which cases undrained collections of pus are usually found at autopsy or when the pericarditis does not clear up satisfactorily and a rather profuse discharge of pus continues from the wound. An instance of the latter type occurred in a boy of five years who had been operated upon several weeks previously. The author again widely exposed the pericardium extrapleurally and carefully incised the sac without preliminary aspiration. Purulent exudate was encountered.

The sixth condition in the author's experience in which he believes pericardiectomy is indicated is that of acute pericarditis of low grade virulence. In a woman of sixty-eight years, he explored the pleural cavity for the cause of an unexplained fever as the roentgenograms had been difficult to interpret, the pericardium, which appeared congested and possibly thickened, was aspirated and turbid yellow fluid was recovered. The culture was later reported

as sterile. The pericardial sac was laid open freely and found to be occupied by fibrinous exudate and small pools of yellowish fluid. The report on the specimen from the pericardium was acute inflammation. No organisms were found in the sections.

The last in the author's series of indications for pericardiectomy is a case of subacute endarteritis complicating a patent ductus arteriosus in which it was thought that the exposure of the ductus for ligation, especially of its posterior not easily attainable aspect, might be facilitated by incision of the pericardium and retraction of the dilated pulmonary artery. This procedure was tried in a woman of thirty years in whom the blood culture was positive for the streptococcus viridans. At operation the mediastinal pleura was incised in the customary manner and the recurrent nerve was visualized beneath the aorta. It soon became evident that dissection under vision would not be possible on the deep surface of the short, extremely wide duct. The pericardium was incised radially and freely over the region of the left auricular appendage, the incision prolonged to the beginning of the ductus and the pulmonary artery was drawn downward and medially. The deep surface of the ductus was visualized and its dissection readily accomplished.

In the discussion HARRINGTON intimated that he does not need to do a pericardiectomy in his patients with a patent ductus because he always obtains adequate exposure through a posterolateral incision which he described quite fully.

JONES cited Gross' objection to opening the pericardium when mobilizing the ductus arteriosus because the trickle of fluid from the sac obscures the field of operation and stated that he himself has not seen a noninfected ductus arteriosus which required the opening of the pericardium for ligation.

HAGERT described a personal experience with herniation of the heart through a large unclosed pericardial opening, which may be combated by turning the patient on or toward the contralateral side.

GRAHAM credited Sauerbruch with first describing the procedure of leaving the pericardium open for drainage into the pleural cavity as in cases of intractable pericardial effusion, and he described a personal experience of this nature.

HEAD described an accident tearing open of the left auricular appendage, incident to the opening and closing of the pericardium. The hemorrhage was finally mastered by grasping the entire appendage with an ovum forceps and ligating it back of the forceps. (The patient made an uneventful recovery except for two or three weeks when he had almost daily attacks of paroxysmal tachycardia.)

DOLLEY said that he believed that some type of drainage with rubber tissue to the outside or into the pleural cavity in cases in which a considerable quantity of serum is likely to form in or in the cavities of the opened pericardium is a necessary safeguard against postoperative cardiac tamponade.

JOHN W. BRENNAN, M.D.

ESOPHAGUS AND MEDIASTINUM

Daniel R. A., Jr.: Congenital Atresia of the Esophagus with Tracheoesophageal Fistula. *Ann. Surg.* 1944, 120: 764.

In the past three years 7 infants with congenital atresia of the esophagus have been admitted to the Vanderbilt University Hospital, Nashville, Tennessee. All of the patients were operated upon and 1 is living at the age of six months.

The successful case was that of a male infant born at term. Thirty-six hours after birth it was noted that the child had an unusually large amount of mucus. At fifty-six hours the diagnosis was suspected and proved with x rays. Operation was performed eighty-four hours after birth. A left posterior extrapleural approach was made under local anesthesia. The blind pouch was isolated and controlled with a silk suture. The lower end connected with the carina. A catheter was inserted through the nose and passed out of the blind loop through a small incision made in the lower end. The lower segment was doubly ligated and separated from the carina. The catheter was inserted into it below the ligature. Silk sutures were used to anastomose the upper end with the lower end below the ligature. The wound was closed and traction applied to the catheter. Gastrostomy was performed seven days later because the catheter became obstructed. Three weeks after the gastrostomy the catheter was removed and dilatations were begun and have been continued at weekly intervals.

The fistula should be exposed and ligated in all cases. An anastomosis is then attempted. In some patients it will not be possible to make the anastomosis. In these cases the upper end is brought out in the neck and a gastrostomy performed.

THOMAS F. THORNTON, JR., M.D.

MISCELLANEOUS

Goldman, A.: Aerial Evacuation of the Thoracic Wounded; Consideration of Effects of Altitude. *U. S. War Med. Bull.* 1944, 43: 685.

Aerial evacuation of the wounded from combat areas has become a common practice in this war. No medical problems have been confronted except in the care of wounds of air-containing organs. In order to determine the effect of aerial evacuation in chest injuries, the author studied 30 such patients. The advantages of air transport were found to be the shortened travel time, a smooth trip, ease of loading and minimal handling. It is possible in the South Pacific area to fly at altitudes of 500 feet, and heights of over 3,000 feet are avoided. Higher altitudes can produce emergencies. All pleuropulmonary wounds are associated with varying degrees of cardiorespiratory disturbance. Altitude tends to increase that disturbance, but significant changes due to altitude are not likely to occur under heights of 3,000 feet. Air entrapped in the body is affected by altitude according to Boyle's law, which states

that the volume of any gas varies inversely with the pressure, provided the absolute temperature remains constant. Lovelace and Hinshaw state that the increase of altitude has the effect of producing considerable increase of either the volume of air in the freely expanding pneumothorax or the positive pressure within the pneumothorax if expansion is restricted. Table I demonstrates the relative volume of gas entrapped in the body at various altitudes.

TABLE I.—GAS ENTRAPPED IN BODY

Volume of gas	Altitude in feet	Barometric pressure mm. Hg.
1.0	0	760
1.2	5,000	63
1.3	10,000	53
1.9	5,000	43
2.4	20,000	35
3.0	5,000	28
4.0	30,000	20
5.4	35,000	16
7.6	40,000	14
8.8	45,000	12

A freely expanding pneumothorax simply expands at higher altitudes, and the amount of expansion can be calculated from this table. In the case of a nonexpanding pneumothorax the positive pressure becomes higher with ascent, and marked pain and dyspnea may occur. This is particularly dangerous since it may cause rupture of adhesions. A closed tension pneumothorax should be decompressed by aspiration or in an emergency by converting it into an open pneumothorax. A sucking wound is best treated by converting it into a closed pneumothorax, and aspirating. Mediastinal and subcutaneous emphysema offers hazards since the entrapped air will also expand and may cause severe obstruction to the contiguous structures. Air entrapped in the pericardium may expand to the extent of causing tamponade. In the case of diaphragmatic hernia the expansion of gas in the stomach and bowel decreases the pulmonary volume and may cause strangulation of the bowel.

Since the weather conditions, mountains and enemy action may force ambulance planes to high altitudes, the flight surgeon should have the equipment and training to manage any emergencies that may occur. If this is done air evacuation offers many advantages. Transportation is usually delayed until pleuropulmonary wounds are stabilized because most severe fresh injuries demonstrate dyspnea, shock, pain, and fear.

THOMAS F. THORNTON, JR., M.D.

Ritvo, M., and Peterson O. S. Jr.: Parasternal Diaphragmatic Hernia. *Am J Roentg* 1944, 53: 399.

Diaphragmatic hernia is defined as the protrusion of any abdominal viscus into the thoracic cavity through an opening in the diaphragm. The following classification of types is suggested:

A. Nontraumatic

1. Congenital
 - a. Esophageal hiatus
 - b. Pleuroperitoneal foramen of Bochdalek
 - c. Dome of diaphragm
 - d. Foramen of Morgagni
 - e. Absence of a portion of the diaphragm
2. Acquired
 - a. Esophageal hiatus
 - b. Pleuroperitoneal foramen
 - c. Foramen of Morgagni

B. Traumatic

1. Blows to abdomen
2. Penetrating wounds
3. Perforation of subphrenic abscess or empyema

Three groups of muscles fuse into a central tendon to form the diaphragm. These muscles arise from the sternum, ribs and lumbocostal arches. Lack of fusion of the sternal and costal muscles forms the so-called foramen of Morgagni with the development of the parasternal diaphragmatic hernia, which is the basis of the present discussion. This type of hernia is exceedingly rare although it was first recognized by Morgagni in 1769. By 1939, a total of 15 cases had been recorded in the literature.

These hernias occur more frequently on the right side because of the more extensive attachment of the pericardium to the left anterior chest than to the right. The contents of the hernia usually compress the omentum and transverse colon. For this reason the barium enema is used in the usual diagnostic roentgen study. The symptoms are usually constipation and pain in the chest, but many hernias cause no symptoms.

X-rays show a density over the lower portion of the right lung field. If the colon is present in the hernia gas may be observed. Barium studies of the stomach usually show no abnormality but varying degrees of displacement of the colon may be visualized.

In the past treatment has been conservative in most instances unless strangulation had occurred.

THOMAS F. THORNTON, JR., M.D.

Holmes, H. R.: A Case of Patent Ductus Arteriosus Associated with Multiple Pulmonary Aneurysms and Infective Endocarditis. *Br J Radiol*, 1944, 17: 374.

The author records a case of patent ductus arteriosus in which there was subacute bacterial endocarditis and multiple aneurysms of the larger branches of the pulmonary artery. The clinical description, roentgenological findings, differential diagnosis, and postmortem findings are given with a discussion.

Ligature of the patent ductus was followed by cessation of the murmur; however, two days later the patient died immediately after a copious hemoptysis.

Left and right anterior oblique films with barium confirmed the findings in the posteroanterior film and showed the absence of auricular enlargement, an apparently normal aorta, and slight enlargement of

the left ventricle. From the changes seen in forced expiration and inspiration films, it was considered that the bilateral radiating opacities were probably caused by pulmonary arterial branches and their local dilatations due to possible aneurysms. The presence of congenital rib anomalies suggested that an associated congenital cardiac lesion might be responsible, in part at least, for the abnormal shadow.

Patent ductus arteriosus is more frequently associated with other cardiovascular anomalies, and there is a known variance in the clinical signs and x-ray appearances. Therefore full roentgenological investigations are essential in the clinical assessment of the indications for timely surgery in the cure of patent ductus arteriosus.

ERIC C. ROBINSON, M.D.

Wolpaw S. E., Higley C. S., and Hauser H. Intrathoracic Hodgkin's Disease. *Am. J. Roentg.*, 1944, 52: 374.

The typical peripheral manifestations of Hodgkin's disease are well known, but the internal disorders, particularly intrathoracic manifestations, are less well recognized. This study includes 55 cases of which 35 (63 per cent) showed intrathoracic involvement. The various types of intrathoracic Hodgkin's disease are (1) mediastinal, (2) parenchymal, (3) pleural, (4) osseous, and (5) cardiac.

The mediastinal variety was the most common in this series since 50 per cent of the cases were in this group. Any of the lymph-node structures in the mediastinum may be involved, but in most cases

localized enlargement of the hilar nodes is present. Occasionally involvement is diffuse.

The parenchymal type occurred in 40 per cent of the series and presented the most confusing diagnostic problems because it varies so much and can easily be mistaken for almost any other type of pulmonary disease. Particularly common is an infiltrative lesion that can easily be mistaken for bronchogenic carcinoma. Nodular lesions are uncommon and simulate metastatic tumors. Peribronchial and bronchial invasion may produce atelectasis like that seen in primary lung tumors. Cavitation occasionally occurs when there is necrosis of tissue with extrusion through the tracheobronchial tree. Tuberculous abscess or cavitory bronchogenic carcinoma may be suspected.

Pleural involvement is quite frequent and usually takes the form of multiple nodules that produce massive effusions which can be confused with tuberculous or carcinoma. The ribs and sternum may show involvement primary or secondary to the lung. The osseous lesion is usually osteolytic. The cardiac type is extremely rare and usually secondary to mediastinal or parenchymal involvement.

Twenty three of the 35 cases were treated by irradiation. Seventeen cases considered to be adequately irradiated showed definite favorable responses of varying degrees. Three patients with adequate, and 2 patients with inadequate dosage showed no favorable response and in 1 case the result was not recorded. The technical aspects of roentgen therapy are discussed.

THOMAS F. THORNTON, JR., M.D.

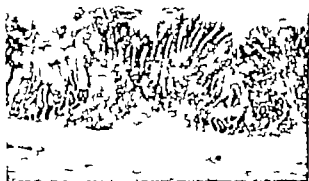


Fig. 3. Two islands of so-called intestinal epithelium.

develops on the basis of gastritis usually hold the theory that it is an atrophic gastritis.

In answer to Crohn's statements MEISSNER asserts again that he has found marked epithelial changes in severe gastritis and believes that they were strictly comparable to well accepted precancerous lesions elsewhere and that it is on this basis only that it is believed reasonable to expect that carcinoma may develop in the stomach from this change.

JOHN W. BRIDGMAN, M.D.

Blagard, J. D., and Overmiller W: Emergency Gastroectomy for Acute Perforation of Carcinoma of the Stomach with Diffuse Soiling of the Free Peritoneal Cavity *Ann Surg* 1944, 120: 326.

Acute perforation of carcinoma of the stomach into the free peritoneal cavity occurs infrequently. It is usually unanticipated and in many instances the malignant character of the perforated ulcer is unrecognized with the result that the case is managed as a benign lesion and treated as such. Routine frozen-section examination of a biopsy from the edge of all gastric perforations would reveal the presence of a neoplasm. Any surgical treatment short of resection in the resectable cases is of doubtful value. But there is the question whether resection be performed as an emergency gastroectomy in the presence of diffuse soiling of the peritoneum or whether it be reserved for a secondary operation contingent upon recovery from the primary operation of simple closure of the perforation.

Because this and other questions relating to this entity can be answered only by the accumulation of many isolated individual experiences it seemed justifiable to the authors to record their experience with a single case and to add a statistical compilation of the reported cases to date. A case report is described in detail. They have collected a series of 217 cases, in which the diagnosis has been established at operation or postmortem examination. In half of these cases no operation had been performed. In only 7 of the 217 cases was it alleged that a correct

diagnosis had been made prior to operation or post mortem examination.

The failure to recognize the presence of carcinoma suggests that the majority of carcinomas which perforate are small and relatively confined lesions, presumably suitable for resection, a premise which is borne out at the autopsy table. In these cases there is, therefore the possibility of considerable salvage of life. Approximately 50 per cent of carcinomas which perforate are otherwise resectable upon the basis of generally accepted standards. For resectable lesions emergency primary gastroectomy is the operation of choice. The results of operative procedures in 115 cases of perforated gastric carcinoma are listed in a table, under procedure, recoveries, and hospital deaths.

EARL C. ROWMAN, M.D.

Rafsky H. A., Katz, H., and Krieger C. L: Varied Clinical Manifestations of Lymphosarcoma of the Stomach. *Gastroenterology* 1944, 1: 297.

This study is based on a series of 12 patients of whom 7 were males and 5 females. Their ages ranged from nineteen to eighty years. All of the patients came to operation. The symptoms of the patients covered a period of from four weeks to three years, with more or less gradual onset, the complaints differing from those of ulcer or perhaps resembling them but on the whole there was no characteristic or typical history to indicate the presence of the disease, nor did the physical examination reveal it. The patients appeared to be chronically ill but did not, as a rule, appear to be undernourished. Thirty three per cent revealed a tumor mass in the abdomen. Roentgenography resulted in a definite diagnosis of lymphosarcoma of the stomach in 4 (33 per cent) and suspicion of neoplastic disease in 6 (50 per cent).

When x ray findings are obtainable they may be grouped as follows: (1) a filling defect with smooth margins; (2) a localized type of filling defect, rounded and smooth when the body of the stomach is involved, and annular when it occurs at the pylorus; (3) a diffuse type of defect involving a large portion of the stomach and simulating carcinoma or fibrous plastica; (4) a defect with the pattern of giant rugae; (5) in the late stages the walls may be somewhat rigid, due to infiltration and yet peristalsis may be sluggish or irregular; (6) gastric retention, which is an uncommon finding; and (7) changes in the size of the stomach.

Gastroscopic findings were not as characteristic of malignancy as those seen in carcinoma of the stomach. Endoscopically in 4 patients there was a marked hypertrophy of the rugal folds and the mucous membrane appeared to be intact although it was somewhat swollen and edematous. The entire gastroscopic field presented a stiffened appearance. Late in the disease flattened ulcerated areas on the crests of the folds were seen. Even at operation, with the surgeon palpating the stomach in the open abdomen, the condition could not always be detected, although later microscopic examination of the resected stomach revealed in some cases that it was involved.

The latest reports on the x ray treatment of lymphosarcoma of the stomach are very encouraging of the 2 types retic lum-cell sarcoma and the small round-cell lymphoma the first gave a less favorable response in treatment.

The details of several illustrative cases are included

JOHN W. BRENNAN, M.D.

McKlitrick, L. S., Moore, F. D. and Warren, R.: Complications and Mortality in Subtotal Gastrectomy for Duodenal Ulcer; Report of a Two-Stage Procedure. *Ann. Surg.* 1944, 120: 531

In this article the hospital morbidity and mortality in 175 subtotal resections done in the period from 1936 to 1941 are analyzed and contrasted with the results in 145 resections done in 1942 and 1943. As one of the many factors producing improvement in the second group a technique for the performance of subtotal gastrectomy in two stages is described. Of the 175 subtotal resections of the stomach (from 1936 through 1941) 55 were performed for gastric ulcer with no deaths. One hundred and twenty four operations were undertaken for duodenal ulcer with 10 deaths a mortality of 8.1 per cent. The various types of operations are shown in a table. The 124 cases of duodenal ulcer were carefully studied from the point of view of fatal and nonfatal complications and the results of this study are grouped in another table.

The experience of the authors suggested that the duodenal stump and its management played an important role in the morbidity and mortality following subtotal resection for duodenal ulcer. In 7 of their 10 fatal cases the infection arose from the duodenal stump. The resection for exclusion as conceived by Finsterer seemed to them to represent the ideal first step of a two-stage procedure, having as its objective the safe removal of the entire lower two-thirds of the stomach. It was anticipated that after from six to twelve weeks had elapsed the inflammatory process around the duodenum would subside, the ulcer probably would heal, and excision of the antral segment could then be safely undertaken. This procedure has now been carried out in 37 cases. It is the authors' opinion that the two-stage gastrectomy will find usefulness for the skilled and experienced gastric surgeon in occasional cases in which the inflammatory fixation of the pylorus and duodenum destroys landmarks and renders adequate duodenal closure difficult or impossible. The operative technique is described in detail and is well illustrated. Complications of the two-stage procedure are enumerated. The answer to the question: Must the antrum always be removed? is an unqualified "yes." This conclusion is based upon three considerations:

1. Edkin's work demonstrating that a substance in the antral mucosa when injected intravenously in dogs, produces a massive gastric secretion even in isolated gastric tissue.

2. The fact that 9 patients known to the authors one of them in this series developed jejunal ulcers

when the antrum was left in for from three to thirty six months after a Finsterer type of procedure.

3. The fact that all of these patients have had their jejunal ulcer cured by antral excision alone or in combination with a higher resection.

During the last two years there has been an improvement in the results in these cases the most important factor in the authors' opinion being the almost complete elimination of those complications secondary to leakage or contamination from the duodenal stump.

EMIL C. ROBITZKE, M.D.

Milpriss, T. W., and Etheridge, F. G.: Chest Complications after Gastric Surgery. *Brit. M. J.* 1944, 2: 466

The authors call attention to the frequency the importance, and the severity of postoperative pulmonary complications in gastric surgery. A report is given of such conditions in 100 consecutive cases. For a correct appraisal of this incidence, some information regarding the condition for which operation was indicated in each instance is necessary. The operative mortality too must be considered, as well as the standards by which the pulmonary complications have been assessed.

Gastrectomy is more difficult when it is done for a peptic ulcer for which a previous operation was performed. Moreover greater difficulties are involved when a bleeding ulcer or a malignancy is present. Accordingly the cases considered are classified as follows: (1) patients with peptic ulcer who had not previously undergone surgery apart from the suture of a perforation (78 patients: 1 fatality); (2) patients who had previously undergone surgery (11 patients: 2 fatalities); (3) patients with complications such as acute hemorrhage (5 patients: 1 fatality); and (4) patients with carcinoma of the stomach (6 patients: no fatalities). From this it will be seen that gastrectomy was performed for the usual indications. Of the 100 patients 4 died.

Physical examination of the chest was routine during the first two or three postoperative days. Any abnormal rise in temperature, pulse or respiration rate suggesting the possibility of a pulmonary complication called for roentgenography. Of the 100 patients, 45 were subjected to roentgenography within the first few days after operation.

Among the primary types of immediate pulmonary complications found are (1) bronchitis (2) lobar atelectasis and (3) lobular or patchy atelectasis. The authors diagnosed bronchitis in patients who had a productive cough with moist sounds in the lungs even though x ray examination showed no abnormality. Lobar atelectasis implies an involvement of one or more lobes a condition which is easily demonstrated by roentgenography. The authors found lobular or patchy atelectasis the most common complication. In most cases physical examination showed that the lower part of the chest on one or both sides was expanding somewhat less fully than normal and auscultation revealed a poor air entry with some adventitious sounds. There would be a

The pathological changes accompanying Meckel's diverticulum depend to a large extent on the anatomic deformities present. These are also briefly mentioned and discussed although the ones most commonly found may be grouped into three categories namely (1) inflammatory type (2) peptic-ulcer type (with or without hemorrhage) and (3) intestinal obstruction type (with or without intussusception). It would appear that another phase of the peptic ulcer type is being seen and not being recognized. This the author believes is the group of diverticula that contain heterotopic gastric mucosa and which, when examined, show no evidence of inflammation or other disease. This condition might be called dyspepsia Meckeli and probably represents a preulcerative condition in the diverticulum or in the marginal portion of the ileum. The best classification is probably that of Greenblatt and his coworkers.

The symptoms and signs that occur from Meckel's diverticulum depend to a great degree on the anatomic disposition of the tissues and the pathological changes involved in the diverticulum. These factors are extremely variable. The signs and symptoms fall into three groups and are described. The treatment of Meckel's diverticulum is surgical, with excision of the diverticulum. Twelve case reports are cited.

EMIL C. ROSENBERG, M.D.

Berger L., and Mirach E.: Bowel Surgery Impressions after 10 Years of Experience. *Am. J. Surg.* 944 66 31

The data and impressions submitted in this report have been derived from a service of eight beds over a five year period. There were a total of 116 patients with disease of the large bowel, of which 12 had chronic ulcerative colitis and 22 had malignancy of the right colon, 10 of the midcolon, 43 of the left colon, and 41 of the rectum, while of the remaining 63 had volvulus, 3 diverticulitis of the sigmoid, and 1 imperforate anus. The diagnosis was based on the symptomatology, the contrast enema and sigmoidoscopy.

"The limits of operability have been extended to the point that only if the bowel is frozen, or the liver studded, is a palliative operation performed. Lymphatic metastases ranked high in all groups of colon cases, varying from 44 to 68 per cent, while vascular metastases varied from 22 to 30 per cent. Emphasis was placed upon the fact that the presence of distant metastases, especially in the liver, did not preclude resection of the local growth. Operability was further influenced to a marked degree by the presence or absence of obstruction. The deaths from acute obstruction occurred solely in those patients with obstruction in the left colon, mainly in the splenic flexure. In this group, with marked obstructive symptoms, death was the rule even though minimal decompressive procedures were utilized. Medical decompression with a Miller Abbott tube was not successful in these acute cases. Cecostomy was preferred to transverse colostomy. In addition

the subacutely obstructed cases which responded to medical decompression and were clinically so improved that no obstructive symptoms were manifested showed dilated loops of bowel at operation. When radical surgery was attempted in this group, the mortality was high and the convalescence very stormy. The lessons learned from this group of patients were that it was better to perform minor preliminary decompressive procedures rather than immediate radical resection, and that operability for the most part depends on whether the patient's bowels are not obstructed plus the intra-abdominal findings.

Preoperative blood transfusions to restore hemoglobin to 70 per cent, plasma transfusions, parenteral amino acids, and additional protein feedings were used to elevate the serum protein to a minimum level of 6 gm. Low blood-chloride levels were also corrected. Determinations of the blood-sugar level were routinely made in all patients with the remark that diabetes was discovered several times in cases in which it had been totally unsuspected. Elevated urea nitrogen is in itself not a contraindication to operation, but its presence almost invariably suggests a stormy postoperative course. Prostatic hypertrophy with chronic urinary obstruction was investigated and if present was treated by staged or transurethral prostatic resection before the major bowel surgery. Various attempts were made to cleanse the bowel and reduce the bacterial flora and fauna of the intestinal tract in uncomplicated cases. The routine at present used consists of (a) preliminary purgation, followed by (b) sodium sulfathiazole. No mechanical cleansing of the bowel was performed. The authors have noted that when they used either sulfanilamide or sulfadiazine spinal anesthesia with procaine was not effective in the usual doses or it was completely ineffective.

Shock was treated prophylactically by routine 1,000 cc. blood transfusions during and immediately after operation.

With the authors' meticulous preoperative rehabilitation of the patients, one-stage procedures became justified in most cases. Anesthesia as individualized to each patient but whenever possible spinal anesthesia was the method of choice. However, colostomy closures were performed under inhalation anesthesia because cleanliness of even the posterior spinal region is always suspect in the presence of an open functioning colostomy.

Of 23 patients with lesions of the right colon, 12 were operable. There were 5 one-stage hemicolectomies with ileotransverse colostomies with 1 death, and 7 Laseky right hemicolectomies with 1 death. In lesions of the midcolon, the operation of choice was a Rankin obstructive resection. Ten patients with this condition were treated and 9 were resectable with no mortality. Carcinoma of the left colon was also treated by a Rankin obstructive resection with delayed establishment of colonic continuity. There were 43 cases of carcinoma of the left colon, 9 of the splenic flexure, 8 of the descending colon, and 26 of the sigmoid. Thirty were operable

with a mortality of 10 per cent. The operation of choice in carcinoma of the rectum was a one-stage combined abdominoperineal amputation of Miles. Eighteen of these patients had a one-stage combined abdominoperineal amputation with 1 death. Ten had a first-stage Lahey procedure. Of this group only 5 returned for the second stage, with 3 deaths. Eleven patients were inoperable and had only palliative colostomies. SAMUEL J. FOOLSON, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Armstrong, C. D., and Carnes, W. H.: Obstruction of the Hepatic Veins (Chiari's Disease). Report of 5 Cases. *Am. J. M. Sc.* 1944, 208, 470.

The authors report 5 cases of a rare disease, hepatic vein thrombosis. Almost 60 cases had been reported. The thrombosis occurs most frequently where the hepatic veins empty into the inferior vena cava, probably because of eddy currents formed at the oblique entering angle. As thrombosis of the hepatic vein is often accompanied by inflammatory changes in the inferior vena cava, it is probable that the two processes are continuous. Hepatic vein thrombosis may be partial or complete, or complete with recanalization. Postmortem examinations reveal a characteristic central necrosis of the liver lobules, congestion of blood in this locality, replacement fibrosis of the liver and splenic enlargement.

Obstruction of the hepatic veins has been equally distributed between males and females. The youngest person was seventeen months and the oldest seventy years of age. It occurs most frequently between the ages of twenty and forty years. It may occur in the acute or chronic form.

Pain over the liver sometimes radiating to the back and shoulders, rapid accumulation of ascites resistant to diuretics, simultaneous enlargement of a smooth-edged liver and spleen, development of a collateral circulation, and edema of the legs suggest obstruction of the hepatic veins. This condition is rarely diagnosed during life as the clinical picture is that of obstruction of the portal vein and hepatic insufficiency.

The authors found 5 instances of hepatic vein obstruction in 11,979 autopsies, an incidence of 0.043 per cent. In 3 cases the thrombosis was unimportant as a cause of death and probably occurred just before the patient died. In 2 cases there was recanalization and some collateral circulation. In 1 case there was a polycythemia.

EARL O. LATIMER, M.D.

MISCELLANEOUS

Gilman, T.: A Critical Evaluation of the Neutral Red Excretion and Acid-Secretion Tests of Gastric Function in Normal Subjects, and in Subjects with Gastric Disorders. *Gastroenterology* 1944, 3, 188.

The recent evidence concerning the wide range of acid secretion by normal subjects as well as the

fluctuations observed in the same subject on different occasions has shaken the confidence of clinicians in the value of determination of the acid secretion as a diagnostic procedure. The method is rapidly losing its popularity. In fact, Schindler and Alvarez have recently expressed opinions which may be regarded as the death knell of fractional gastric analysis as a clinical test. The present investigation confirms the opinions recorded by numerous investigators concerning the limitations of the study of acid secretion in the diagnosis of gastric disorders but provides information which promises a new lease of life to a modified form of gastric analysis in the clinic.

In this study it has been established (1) that the excretion of neutral red by the normal gastric mucosa is constant in the same subject on different occasions (2) that disturbances in dye excretion can be easily recognized and (3) that a disturbed neutral red excretion can be regarded as evidence of gastric dysfunction. For these reasons alone, this test deserves recognition as a diagnostic procedure in the clinic.

Moreover, the modified neutral-red test has other qualities which make it invaluable both in the clinic and in the laboratory. It is simple, inexpensive, time-saving, free from unpleasant reactions and above all, it is extremely sensitive.

The improved neutral-red-excretion test, when the rate of excretion and concentration as well as the intensity to which the injected neutral red can be concentrated, are recorded, has been shown to be an excellent indicator of the excretory function of the gastric mucosa.

This test has been applied to 50 individuals with apparently normal gastric function and standards of normality have been suggested.

In 15 of these normal subjects both neutral red excretion and acid secretion were examined repeatedly over a period varying from one week to six months. These repeated studies revealed that the acid secretion fluctuated considerably in the same subject while the excretion of neutral-red remained remarkably constant.

From the study of 500 cases with gastric dysfunction criteria of abnormal neutral red excretion expressed quantitatively have been tentatively suggested. A comparison of the tests for neutral red and acid secretions revealed that the neutral red test is not only reliable but is also more sensitive than the acid-secretion test as an indicator of gastric function.

Acid secretion and dye excretion do not necessarily parallel one another either in healthy or abnormal stomachs. It is suggested that acid secretion and dye excretion are indicators of two apparently independent functions of the gastric mucosa.

In view of its simplicity, reliability and sensitivity the neutral red test can be recommended as a means of obtaining valuable information concerning the functions of the gastric mucosa both in the clinic and in experimental studies.

HARRY W. FINE, M.D.

Cleland, J. B.: *The Length of the Small Intestine.*
Med. J. Australia, 1944 2 359.

The considerable variation in the length of the small intestine is the subject matter of this article. Naturally with a variation in the length of the small intestine there is also a considerable variation in the amount of area occupied by its mucosa.

One would be led to suppose that with such a difference in area there might be a concomitant effect upon the physiology of the subject. However persons with short intestines do not in any way appear to be handicapped during life. Whatever effect the difference in area of the small intestine might produce would now seem to be a matter of quite useless speculation.

In 1941 quite by chance the author who is professor of Pathology at the University of Adelaide Australia happened to notice during the course of a postmortem examination on a woman, aged fifty years that the small intestine seemed very short. As it was detached he proceeded to measure it and found that it was only 15 feet long from the termination of the duodenum to the cecum. This finding led him to make a series of measurements of the jejunum and ileum in more than 100 bodies. His observations showed that remarkable variations existed, ranging from 13 feet (in 2 cases) to 37 feet. The intestine (jejunum and ileum only) was measured after having been detached from the mesentery as close as possible to the intestine itself in such a way that the gut scissors could rapidly slit up the lumen. Probably a number of small kinks were left varying from subject to subject so that all the measurements probably are somewhat less than the actual length.

Arranged in order (inches being neglected) the length of the small intestine in 100 subjects of both sexes was 13 feet in 2 15 feet in 2 16 feet in 4 17 feet in 2 18 feet in 3 19 feet in 4 20 feet in 3 21 feet in 12 22 feet in 7 23 feet in 16 24 feet in 5 25 feet in 6 26 feet in 13 27 feet in 9 28 feet

in 5 29 feet in 2 30 feet in 1 31 feet in 1 33 feet in 1 35 feet in 1 and 37 feet in 1

The author carefully lists the results of measurements in 60 male subjects and also in 40 female subjects. The figures show that the small intestine may be quite short in both males and females. However, whereas 5 of 60 male subjects had a small intestine of 30 feet in length or more none of the 40 female subjects had a small intestine longer than 29 feet. The length did not seem to bear any definite relationship to the length or size of the subject. Even children may have a longer small intestine than some adults. In a boy aged fourteen years the small intestine measured 28 feet in length. In a girl, aged nine years the measurement was 19 feet, 6 inches and in a male infant aged nine weeks, a measurement of 16 feet 4 inches was found.

The author made a careful check-up in the cases of both the lowest and the highest measurements to ascertain what connection, if any, could be found between the diseases from which these subjects suffered and the length of the jejunum and ileum. It was impossible to determine whether disease conditions had any bearing on the length of the small intestine or vice versa.

Nature does indeed present strange incongruities. For example an examination of the bodies of two full-blooded Australian natives gave the following findings. In a woman aged twenty two years, the small intestine measured 21 feet 6 inches in a man, aged thirty five years, the length was 16 feet, 6 inches. In a female half-caste, aged thirty five years, the small intestine was 28 feet long, and in a half-caste boy aged twelve years it was 21 feet, 6 inches long.

Surprising as these variations in the length of the small intestine are it seems even more surprising to find that this difference in area seems to have no effect upon the physiology of the subject, nor upon the disease which caused the death of the subject.

MATTHEW J. SCURRY, M.D.

GYNECOLOGY

EXTERNAL GENITALIA

Quinet, A. A. Vaginal Cytology in Premature Puberty (Citologia vaginal na puberdade precoce) *An. Brasil gín.* 1944, 18 102

In newborn infants the organism is impregnated with maternal follicular hormones and the cells of the vagina are therefore estrogenic in type. They are predominantly well defined squamous polygonal cells with a transparent cytoplasm some of them with granules arranged around the nucleus which is generally pyknotic, well defined and small in comparison with the volume of cytoplasm. From the twenty first day on the type of cells changes. The cells become round or oval with large nuclei and there is an abundance of mucus and of leucocytes. Some of the cells are surrounded by a translucent halo.

The author studied the vaginal cells in 3 little girls who showed precocious puberty. They were three years and seven months, seven years and eight months and four years and two months of age, respectively and showed well developed sexual characteristics. Though they were at an age when the second type of cells described would ordinarily predominate they revealed a predominance of the estrogenic, squamous polygonal cells. A similar type of cells can be produced in girls before puberty by the administration of estrogenic hormones.

There was another peculiar characteristic in the cells of these cases. There was a dark line running through the cells in the oval ones along the long axis and in the round ones near the center of the cell. This line seemed to be caused by a condensation of the nuclear chromatin, and it was found chiefly in the most superficial cells of the stratum spinosum.

AUDREY G. MORROW M.D.

Jeffcoate T. N. A., Davis, T. B. and Harrison, G. V.: Intraepidermal Carcinoma (Bowen's Disease) of the Vulva (A Report on 2 Cases) *J. Obst. Gyn. Brit. Empire* 1944, 51 377

According to Knight, the histological criteria for the diagnosis of Bowen's disease are (a) hyperkeratosis and parakeratosis (b) acanthosis with marked thickening of the rete malpighii which appear club-shaped (c) loss of stratification of the individual cells with disorientation, (d) the presence of nuclear clumping, "corps ronds" nuclear grains and mitotic figures (e) an intact basement membrane and (f) marked vascularity of the subpapillary zone with round-cell infiltration. He points out that it is usually necessary to examine several sections before finding all these features.

The appearance of the lesion to the naked eye shows some variation, but typically it is a dull red raw area with a clearly defined circinate or serpiginous outline. The area is on the same level as the

surrounding skin or at most, is only slightly raised but there is a sharp line of demarcation between the healthy and diseased tissues. The surface is moist but may become encrusted in part the appearance of the lesion being very similar to that of Paget's disease of the nipple. It does not show any of the usual characteristics of malignancy there is no friability or fixation and metastases in lymphatic glands or elsewhere are rare. It may be confused with eczema or with tuberculous or other ulcers and Knight points out that when it occurs on the vulva it may be mistaken for kraurosis or leucoplakia. Indeed, the latter may occur with Bowen's disease.

Clinically the disease runs a slow course, often lasting many years. It sometimes heals spontaneously in the central areas while it advances at the periphery. It can at any time, however change into a frank epithelioma and this is true especially when it encroaches on mucous membranes. At such sites the change into epithelioma with rapid spread and the development of metastases are common.

On the vulva the lesion occurs at any age, before or after the menopause the ages for recorded cases vary from twenty five to seventy three years with an average of approximately fifty years. In the second case reported here, however the patient was eighty-one years old. The symptoms produced are pain and pruritus the area often being extremely tender. In long-standing cases a history of remissions and exacerbations is the rule.

Two cases of intraepidermal carcinoma (Bowen's disease) of the vulva are described in detail. In the first patient the lesion ultimately spread to the vagina and immediately changed into epithelioma which rapidly assumed the most malignant characters. The clinical features of this condition are described, and the diagnosis etiology and treatment discussed. Special reference is made to its pathology and its relation to Paget's disease of the vulva. It is suggested that cases previously described as Paget's disease have in fact been cases of Bowen's disease and it is recommended that the name "Paget's disease" be restricted to the well known lesion of the nipple. The results of treatment in these 2 cases also substantiate other reports that the use of radium is not satisfactory and that excision of the affected area is preferable. In neither of these cases was the growth process arrested by radium application.

CHARLES BARON M.D.

MISCELLANEOUS

Davis, A.: The Treatment of Amenorrhea with Combined Anterior Pituitary Follicle-Stimulating Hormone and Chorionic Gonadotropin *J. Obst. Gyn. Brit. Empire*, 1944, 51 401

The author cites experimental evidence of the value of the combination of chorionic gonadotropin

and pituitary follicle-stimulating hormone, and states that it is more potent than either of its individual constituents as a gonadal stimulant. Twenty-seven patients with amenorrhea were treated by the preparation synapoldin.

After the mechanism of menstruation was discussed the rationale of treatment of functional amenorrhea with pituitary or pituitarylike gonadotropins rather than by substitution therapy with estrogen and/or progesterone, was emphasized.

Clinical classification of amenorrhea, based on the organ presumably primarily responsible, is presented.

The dosage used was 1 cc. of synapoldin given intramuscularly three times weekly for three weeks after careful examination had been made to determine the cause of the amenorrhea. This examination included the basal metabolic rate roentgenograms of the pituitary fossa, diagnostic curettage, and hystero-graphy with lipiodol. The majority of the patients were of the primary pituitary type showing the characteristics of a mild Froehlich syndrome.

Occasionally gross enlargement of the ovary was seen as a complication. This, however gradually subsided after treatment was discontinued.

Results showed a permanent cure of 14 of the 27 cases temporary improvement in 6 and no improvement in the remainder. The duration of the previous amenorrhea did not seem to affect the result.

The author believes this preparation is the best so far offered for amenorrhea especially that of the pituitary type with a mild Froehlich syndrome. Frequent examinations are necessary to control ovarian hypertrophy. Hemorrhage is a contra-indication to continuance of the treatment.

T. FLOYD BELL, M.D.

Thomas, R. B. and Cannefax, G. R.: Sulfonamide Therapy of Gonorrhea. *J Am M Ass.*, 1944, 136: 63.

The authors report the results of their experience in the treatment of gonorrhea in 555 women (200 negro and 355 white). All were hospitalized and under constant observation during the period of treatment.

The histories were of little value in making the diagnosis since the most frequent symptoms in the patients with gonorrhea, as well as in those without infection were lower abdominal pain and vaginal discharge. Nonspecific cervicitis and vaginitis were frequently encountered. On admission, cervical and urethral cultures and smears were taken in all cases. Rectal and Bartholin smears were taken only when there was an indication of infection in these areas. Beginning five days after treatment cultures were taken every other day and if they were negative until an uninterrupted total of 6 cultures had been examined.

All patients were started on sulfathiazole with the exception of a few who were given sulfadiazine. The

TABLE I.—RESULTS OF SULFONAMIDE TREATMENT BY RACIAL GROUP

Method of treatment	White (555)				Negro (200)			
	Cure		Failure		Cure		Failure	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
1st course, 5 day	174	66	141	49	182	90	20	10
2d course, 5 day	34	27	94	73	28	23	9	7
Total cures	208	70			210	83		
Total failures			207	70			9	4

total dosage amounted to 20 gm. 1 gm. being given four times daily for five days. Some patients were given a larger amount of the drug. If five days after completion of the treatment the cultures still were positive, a second course was given. Patients who did not then become negative were considered to be sulfonamide-resistant and were given foreign-protein therapy and sulfonamides. If this failed, artificial fever therapy with a sulfonamide, or penicillin (10,000 units every three hours, for a total of 60,000 units) was used.

The results obtained paralleled those for males. Seventy-one per cent of the patients were cured by the first course of sulfonamides, and 81 per cent were cured by either one or two courses of treatment. About one-third of those who were subjected to foreign protein therapy and 23 of 25 treated by artificial fever gave negative cultures. Ninety-four per cent of the penicillin-treated sulfonamide-resistant cases were cured following the administration of a total of 60,000 units.

The disease was much easier to cure in the negro than in the white patient (Table I). In no negro was it necessary to use artificial fever and in only 1 instance was penicillin used.

In some complications of the adnexa and Bartholin's glands the sulfonamides failed to produce a cure, although clinical and symptomatic improvement was noted despite the fact that the cultures remained positive.

There were few cases of sulfonamide reaction. In 3 patients the ureters became blocked during hot weather. This was prevented subsequently by increasing the fluid intake. Three patients developed hematuria.

J. ROBERT WILLIAMS, M.D.

Greenblatt, R. B. and Street, A. R.: Penicillin for the Treatment of Chlamydia-resistant Gonorrhea in the Female. *J Am M Ass.*, 1944, 136: 61.

The sulfonamides are effective in curing a little better than 55 per cent of the cases of gonorrhea in the female. One hundred and nine patients were treated with penicillin and of these 93 per cent had had one or more courses of sulfonamides. The total dosage of penicillin varied from 60,000 to 150,000 units. No untoward reactions were encountered.

Five patients received a second course of penicillin because of relapse. The second round of penicillin varied from 120,000 to 300,000 units. These patients remained negative after the second course of therapy.

Dosage should not be reduced to the minimum necessary for good results but should be maintained at a sufficiently high level so that the development of penicillin resistant strains may be thwarted. To this end it is recommended that 150,000 units be used.

T FLOYD BELL, M.D.

Phaneuf, L. E.: The Changes in Operative Gynecology during the Last Quarter-Century. *J. Am. Med. Ass.*, 1944, 136: 139.

The last quarter of a century has shown much progress in surgical technique with emphasis on careful dissection and ligation of individual vessels with fine material rather than mass ligation of the tissues. The treatment of carcinoma of the uterine cervix has changed from surgery to irradiation. However, a few gynecologists have again turned to surgery in well selected cases. Improvement in technique, and the use of blood transfusions and of the sulfonamides has lowered the mortality from the Wertheim operation.

The treatment of carcinoma of the uterine corpus and fundus still remains surgical with ablation of the adnexa, with or without preoperative radium and postoperative high voltage x ray therapy. Improvement here has also come through early diagnosis by means of curettage for women who bleed irregularly at or after the menopause.

Improvement in the operation of myomectomy has resulted in more conservative surgery of fibroids. In young women who are still in the childbearing age, the advantage of myomectomy rests in the fact that the functions of menstruation and reproduction are not abolished.

Supravaginal hysterectomy still remains the type of operation most often performed. However an increasing number of gynecologists have turned to panhysterectomy as a prophylactic means against carcinoma of the cervical stump. The author almost entirely performs the total operation. If radium or x rays are used for fibroids a thorough curettage of

the uterus should be done to rule out malignant disease. In the young whose ovaries should be conserved and in the good surgical risks surgery is still accepted as the better method of treatment.

During the last two decades vaginal hysterectomy has been reborn and its performance in all gynecological services is now commonplace. Since it plays such an important role in gynecology it is not likely to be again abandoned.

Originally vesicovaginal fistulas were the result of the trauma of childbirth. With the increase of pelvic operations the so-called surgical fistulas now greatly outnumber the obstetric. The latter offer greater difficulty in closure. Two helpful adjuncts to the operation are the Schuchardt incision, and suprapubic cystostomy. Metal wire still has a place in the repair of vesicovaginal fistulas.

The current and useful method of cauterization of the cervix has resulted in the less frequent performance of trachelorrhaphy and amputation of the cervix.

A significant advance has been made in the surgical treatment of uterine prolapse, cystocele and rectocele because of a better understanding of the structures that hold the pelvic viscera in their normal position. The supportive structures are exposed by layer dissection rather than by superficial dissection of the surface mucous membrane of the vagina. Better operative results have been secured. Uterine suspension and fixation have definitely decreased in frequency.

The treatment of pelvic inflammatory disease is more conservative. The sulfonamides are decreasing the incidence of this condition. Puerperal sepsis still heads the list of causes of maternal deaths in this country. Here again prophylactic measures are beneficial and the sulfonamide drugs are valuable.

Progress with ovarian tumors has been due to better classification and the recognition of certain of the rare ovarian new growths. There are no great differences of opinion as to the operative management of ovarian tumors. True neoplasms of the ovary should be removed surgically because of the danger of malignant degeneration. This should be done when the diagnosis has been established.

T FLOYD BELL, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Herman L., and Greene L. B.: Pregnancy after Bilateral Ureteral Transplantation; Report of a Case after Bilateral Ureterocutaneous Transplantation. *J Urol* Balt., 94, 52-300.

Very few pregnancies after ureteral transplantation have been reported, as might be anticipated from the comparative rarity of this operation and, what is equally important, the disinclination of women with serious physical defects to get married. Congenital malformations of the female genitalia which preclude either impregnation or successful gestation rarely occur in association with exstrophy or other maldevelopment of the bladder and contribute little to sterility in the type of case under discussion. Randall and Hardwick in 1934 found in the literature up to 1934 reports of 28 children born to 20 mothers with exstrophy of the bladder. Not all of the mothers had had ureterointestinal anastomoses. The literature since 1934 contains only 1 case report.

The deliveries in 21 of the 28 cases collected by Randall and Hardwick were normal and without unusual incident. It would seem that cesarean section is rarely necessary in women who have submitted to

ureterointestinal anastomosis for exstrophy of the bladder.

Females with acquired urinary lesions requiring ureteral transplantations are often beyond the child-bearing period or incapable of gestation because of the seriousness of the disease. The opportunity, therefore for pregnancy following this operation are rare. The authors describe the case of a fully matured Polish girl aged nineteen years, who had had a tumor (probably a meningocoele) removed from the base of her spine at the age of six months. Her first admission to the urological department of the Pennsylvania Hospital was on July 19, 1939. She had never experienced the desire to void and had had constant dripping of the urine from the urethra, except on a few occasions when lying quietly on her right side or walking carefully also there had been rectal incontinence when the bowel movements were liquid.

After numerous methods of treatment had been tried unsuccessfully cutaneous ureterostomy was carried out. Several months after this she married and soon became pregnant. On February 9, 1944 at about the eighth month of pregnancy she went into labor and was quickly delivered of a dead hydrocephalic infant. This obviated the necessity for cesarean section which had been anticipated as a means of preventing rectal and other possible injuries. Bilateral retrograde pyelograms made shortly before delivery illustrated the very satisfactory condition of the renal pelvis which had escaped dilatation, including that incident to pregnancy. The kidneys were normal in function and only mildly infected.

DANIEL G. MORROW, M.D.

Finn, W. F.: Thrombocytopenic Purpura in Pregnancy. *Am. J. Obst.* 94, 48-497.

Purpura hemorrhagica is at best a rare disease, but its coexistence with pregnancy is rarer still. The author gives in detail the classification, symptoms, diagnosis and treatment of the disease. Three cases are reported in detail. The patient usually comes to the doctor complaining of bleeding from the mouth, epistaxis, or hematuria. The acute phase is more common in early life and the patient may progress to death from anemia or intracranial hemorrhage. The most striking physical sign is the presence of purpuric spots varying in size from the point of a pin to the head of a pin. Infection of the mouth at Vincent's organisms is a common association.

The treatment of thrombocytopenic purpura is both medical and surgical. In the acute phase, the patient is placed in bed, a high protein and high vitamin antianemic diet is given, and fœcol is administered. Blood, citrated and fresh, or red-cell transfusions are given to control the bleeding, to keep the red-cell count above 2,000,000, and to keep the blood pressure above 90. Within the past year



Fig. Retrograde pyelogram at eighth month of pregnancy. Note normality of pelvic outflow. Head of fetus is enlarged as result of hydrocephalus.

intrus pectin in dosage of from 3 to 9 gm. a day has been recommended by Isaacs. This checks the bleeding without affecting the platelet count. Either spontaneously or because of this therapy the acute phase will subside. In this interval foci of infection are removed or splenectomy is done. Splenectomy is contraindicated if there is any doubt of the diagnosis, if there is a history of recent drug ingestion, and above all, if sternal puncture fails to reveal megakaryocytes in the bone marrow.

How is the child affected by the thrombocytopenic purpura of the mother? Mosher states that 50 per cent of the infants die in utero or after delivery. Burnett and Klass, at the other extreme, believe that if the fetus develops purpura, it is not essential thrombocytopenic purpura but symptomatic purpura or it is due to a familial platelet defect. Rushmore, in 1925 reported 7 instances in which purpura was present in both mother and child. The author adds 3 more examples of this: the first baby dying of congenital thrombocytopenic purpura and the second living (also an example of congenital thrombocytopenic purpura). EDWARD L. CORNELL, M.D.

James, H. W. Jr and Neill, W. Jr: The Treatment of Carcinoma of the Cervix during Pregnancy. *Am. J. Obst.*, 1944 48 447

In formulating a plan for a clinical situation as rare as the association of pregnancy and carcinoma of the cervix, one must draw upon the collective experience of the literature as well as upon one's own cases.

The authors believe that a general rule for the handling of these cases must take into account the obstetric and social background as expressed in the desire of the prospective parents for the child, as well as the extent of the disease. If there are other children, or if the parents do not care to assume the ever present risk of an abnormal child, they see no reason to advise any course except interruption of the pregnancy and adequate irradiation therapy.

The risk of an abnormal fetus cannot be statistically stated at the present time with certainty but it seems probable that its upper limit is 20 per cent. If the parents and physician for any reason wish to assume this risk, it is justifiable to proceed with irradiation during pregnancy with a view to obtaining a living child at term. If the pregnancy is at the fifth month or beyond the risk of an abnormal child is substantially less. The mother's prognosis is intimately related to the clinical extent of the disease. The general experience has been that most cases are discovered early and the prognosis has been parallel but somewhat poorer than for corresponding but uncomplicated groups.

If treatment during pregnancy with a view to obtaining a normal living child at term is decided upon certain points in technique may be stressed. It is important that no high voltage roentgen ray therapy be employed because of the obvious dangers of substantial depth dosage in the region of the developing child. The authors omit the use of tubes within the

cervical canal. This is done for the twofold purpose of securing all possible distance from the baby and also to guard against the onset of labor by dilatation of the cervix. The entire treatment is carried out with tubes held in a cloth plaque against the cervix. The authors have preferred to use a large amount of radium for a correspondingly short period of time. In the 11 cases reported the dose varied from 1 614 mc. hr to 3 925 mc.

The prognosis of carcinoma diagnosed at term and treated by cesarean section plus panhysterectomy or irradiation is grave. This is in a large measure due to failure of the attending physician to suspect the diagnosis and apply such simple clinical methods as speculum examination and biopsy even in the presence of vaginal bleeding during pregnancy.

EDWARD L. CORNELL, M.D.

LABOR AND ITS COMPLICATIONS

Mackie, M. A.: Comparison between Surgical Induction of Labor by Means of the Rectal Tube and Surgical Induction of Labor by Artificial Rupture of the Membranes. *Statistical Survey Med. J. Australia* 1944, 2 458.

In an endeavor to discover the more efficient method of surgical induction of labor the author carried out a statistical survey of the results obtained by rectal tube induction and by artificial rupture of the membranes. Pregnancy had advanced to at least twenty-eight weeks in every case considered and all cases in which either method was attempted have been included. During this period there were 278 cases of tubal induction and 393 cases of artificial rupture of the membranes.

Toxemia was the indication for induction in 88 per cent of the cases in which a rectal tube was used and in 82 per cent of those in which induction was accomplished by artificial rupture of the membranes. Seven maternal deaths (a mortality rate of 2.5 per cent) followed tubal induction while only 2 deaths (a mortality rate of 0.5 per cent) followed induction by artificial rupture of the membranes. Five of the deaths which followed tubal induction were due to infection and the 2 others were due to obstetric shock after normal deliveries. The 2 deaths which followed artificial rupture of the membranes were due directly to the primary disease. The condition became morbid during the puerperium in 17.2 per cent of the patients in whom labor was induced by rectal tube, compared with this finding in but 13.5 per cent of those in whom labor was induced by artificial rupture of the membranes.

In this series the total fetal mortality rate for tubal induction was 37.2 per cent while the total fetal mortality rate for artificial rupture of the membranes was 19.2 per cent.

When the cases are divided into two groups—(1) those with less than thirty-four weeks of gestation and (2) those with thirty-four weeks of gestation or more—it is shown that in group 1 the fetal mortality rate was 70 per cent following tubal induction and

72 per cent following artificial rupture of the membranes and in group 2 it was 23.4 per cent following tubal induction and 14.1 per cent following artificial rupture of the membranes.

The time from artificial rupture of the membranes to delivery was less than that from tubal induction to delivery in all groups. The average time from induction to delivery after the insertion of a rectal tube was forty two hours while that from artificial rupture of the membranes to delivery was twenty hours.

With regard to tubal induction, 5 inductions were unsuccessful, 1 patient being delivered by lower segment cesarean section and 4 requiring subsequent artificial rupture of the membranes to induce labor. In 1 case prolapse of the umbilical cord occurred.

Artificial rupture of the membranes was unsuccessful in 3 cases and both patients were delivered by lower-segment cesarean section. Prolapse of the umbilical cord occurred 3 times.

This statistical survey indicates that the results of artificial rupture of the membranes are immeasurably superior to those of tubal induction.

DANIEL G. MCCARTHY, M.D.

NEWBORN

Hennessey, J. P.: True Knots of the Umbilical Cord. *Am. J. Obst.*, 944, 48, 518.

True knots of the umbilical cord are not infrequent and are occasionally of a complicated nature. They are usually harmless, since they are rarely pulled tightly enough in utero to obliterate completely the lumen of the vessels, or to cause the death of the fetus. They usually result from the active movement of the child.



Fig. 1. True knots of the umbilical cord.

According to von Winckel, two conditions are necessary for their formation: a cord which in length exceeds twice the distance from the umbilicus to the vertex, and a small fetus or a large quantity of liquor amnii, which ensures mobility of the former. No doubt in many cases the knot remains open until labor begins when the tension imparted to the cord by the descent of the fetus closes it. When the knot has been tightened during pregnancy distortion of the cord will persist even after it has been untied because of the effect of the continued pressure on Wharton's jelly but if it has formed only during delivery it can easily be straightened out. Although it is possible for the knot to become so tightly drawn as to cause a partial or complete obstruction of the cord circulation, this occurs very rarely.

Seven original cases are described, and a tabulation of 32 cases from the literature, supplementing the table published by Browne, is given. There were 2 antenatal deaths of the fetuses. In each case there was one true knot drawn tightly. In 2 other cases there were 2 true knots in the cord.

EDWARD L. CORNELL, M.D.

Anderson, N. A., and Nelson, W. E.: Clinical Observations in the Treatment of Epidemic Diarrhea of the Newborn. *J. Pediatr.*, 5, 1944, 25, 3, 9.

A review of the literature on epidemic diarrhea of the newborn revealed an average fatality of 43 per cent. In this article the therapy of 28 cases of epidemic diarrhea is discussed.

In the early neonatal period the frequency and character of the stools is so variable that the diagnosis of epidemic diarrhea is often difficult. Unexplained diarrhea in any infant or diarrhea in 3 or more infants calls for isolation.

Twenty-eight of 76 term infants and 4 of 9 premature infants who were exposed developed the disease within a period of seven days. Twenty-eight of the 32 infected infants were treated. Seven were considered critically, 8 seriously, 8 moderately and 5 mildly ill. One death occurred in a seventeen-day-old premature infant.

Stool cultures revealed only one organism of any possible significance. This was a para-aerogen type of paracolon bacillus. Loss of weight was characteristic, most marked in the severe cases, and often preceded other clinical manifestations of the disease. Other clinical characteristics were general toxic diarrhea, and in the severe cases a low carbon-dioxide-combining power of the blood.

Treatment of these infants consisted of oral administration of a mixture of glucose and Ringer's solution, parenteral administration of additional fluids, correction of acidosis by the parenteral administration of alkali, oral administration of ascorbic acid and thiamine chloride, blood and plasma infusions as indicated, and, in addition, the administration of succinylsulfathiazole (1 gr. every four hours).

Acidosis was corrected by the administration of a 5 per cent solution of sodium bicarbonate or by the

intravenous and/or subcutaneous administration of 11/6 sodium-lactate solution in calculated amounts. Clinical improvement was noted during or shortly after the administration of alkali. Oral feedings were gradually restored to normal as the infants improved.

In discussing the benefits of this therapy the authors pointed out the fact that control cases were impossible. However the parenteral use of fluids was considered essential. The rapid improvement in acidotic infants after the administration of parenteral alkali impressed the authors in respect to this type of therapy. Succinylsulfathiazole had no noticeable effect on the disease.

JAMES F. DONOFRY, M.D.

MISCELLANEOUS

Lentz, J. W., Ingraham, N. R., Jr., Beerman H., and Stokes, J. L.: Penicillin in the Prevention and Treatment of Congenital Syphilis. *J. Am. M. Ass.*, 1944, 126: 408.

Twelve pregnant women with early symptomatic syphilis and 2 with early latent syphilis, none of whom had previously received any type of anti-syphilitic treatment, were given intramuscular injections of sodium penicillin at four hour intervals in doses of from 25,000 to 50,000 units dissolved in 1 cc. of sterile saline solution, the course continuing for a period of approximately eight days until a total dosage of from 1,200,000 to 2,500,000 Oxford units had been given. In 9 infants with early congenital syphilis neither they nor their mothers having received other anti-syphilitics the same technique of treatment was used for the same period of time, with the difference that the individual doses were so regulated that in 4 cases the total injections ranged between 16,000 and 19,000 units, and the remaining 3 dosages were 2,935, 10,631 and 11,111

units per pound of body weight, respectively. Two of the 9 children died prior to completion of the treatment, these deaths however were not ascribed to the penicillin.

All 14 pregnancies are included in this report merely to show that the higher dosages are well tolerated by the pregnant women and that apparently the highest amount (2,400,000 Oxford units) should be used when the physical condition is satisfactory. Seven of the 14 women (6 with early initially symptomatic syphilis, and 1 with early latent syphilis) have so far delivered and these cases are reported in some detail. None of these 7 women started penicillin prior to the mid-term period of their pregnancies, and none had attained seronegativity at term yet all the infants seemed healthy. 4 were seronegative at birth and 3 became negative in less than a month postpartum and have remained so for short periods of observation. Roentgenograms of the long bones of 4 of the infants were taken both at birth and at the age of six weeks or later in each instance they were normal.

Three of the infants with early congenital syphilis have been followed up long enough to make a report possible (ninety-nine, ninety-seven and seventy-nine days, respectively after administration of the sodium penicillin). All 3 infants had relatively high blood serologic titers initially but these dropped sharply to normal in 1 and to relatively low levels in the 2 others (3½ unit and 8 units respectively), all became clinically normal to physical examination. The 2 infants who showed definite roentgenographic changes of syphilitic osteochondritis and periostitis have resumed approximately normal bone development.

In conclusion the authors urge caution in initiation of the penicillin treatment because of the Herxheimer reaction just as in other anti-syphilitic medication.

JOHN W. BRECKMAN, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY AND URETER

Colby F. H.: Renal Complications of Reiter's Disease. *J. Urol.*, Balt., 1944, 51: 415.

The author's review of 3 cases gives the essential features of the syndrome known as Reiter's disease. All 3 cases occurred in young males. The typical triad of urethritis, conjunctivitis and arthritis was present. There was insufficient evidence to show that the disease was contracted by sexual exposure. Bacteriology has failed to identify the causative agent. The course of the disease is unaffected by any known therapy including penicillin. Instances of permanent joint disability are rare although a few are reported. Recurrent eye, joint, and urinary symptoms may occur and severe renal complications may be encountered. JOHN A. LOFF, M.D.

BLADDER, URETHRA, AND PENIS

Donaldson, S. W., and Ratliff, R. K.: Extravesical Lesions Causing Bladder Neck Obstruction. *Radiology* 1944, 43: 319.

The authors comment upon the lack of reports of bladder neck obstruction due to extravesical causes. During the past two years there have been 5 cases of this type treated by the authors. Three women had complete urinary retention due to fibroids of the uterus associated with uterine ptosis in 2 cases. Recovery was complete in these cases following hysterectomy. One male who had a sacral chordoma which caused vesical neck obstruction was given a permanent suprapubic cystostomy and a male who had a sarcoma of the pelvis which caused acute retention of the urine died in the hospital.

It is believed that extravesical lesions causing obstruction at the bladder neck should offer little difficulty in diagnosis. They should be suspected if the cystoscopic examination is negative in the presence of a pelvic mass which persists after the bladder is emptied. The extravesical tumors usually do not cause the rectal symptoms and venous stasis which accompany most retroperitoneal tumors, and for that reason the diagnosis of such lesions may be arrived at by the process of elimination. Careful pelvic and rectal examinations together with cystograms usually establish the diagnosis.

Osteomyelitis with soft-tissue abscess has been observed to cause bladder distortion but never obstruction. Fractures of the pelvis cause obstruction by contusion or rupture rather than by pressure. Lesions of the lower bowel involving the rectum, even though far advanced, rarely cause vesical neck obstruction. This is probably due to the mobility of the gut and to the pelvic fascia, which serves as an effective barrier.

Treatment in cases of bladder-neck obstruction should be instituted in order to relieve the obstruc-

tion and to restore the urinary organs to as near normal function as possible. Early treatment is indicated in order that kidney damage may not become so severe that it cannot be remedied. The blood urea and renal function should be determined.

Cystograms of excellent diagnostic value are reproduced in the original article.

DONALD F. McDONALD, M.D.

GENITAL ORGANS

Frame, E. G., and Jewett, H. J.: The Excretion of 17 Ketosteroids in Carcinoma of the Prostate: Personal Experiences. *J. Urol.* Balt., 1944, 53: 339.

The total excretion of urinary 17-ketosteroids has been determined in 16 cases of carcinoma of the prostate and compared with that of 8 controls in a similar age group. Five of the patients with carcinoma had been castrated from ten to twenty-four months previously. In all cases the total 17-ketosteroids were separated into alpha and beta fractions since the literature contains suggestions that such separations may be of clinical importance.

The results indicate that the total 17 ketosteroid excretion in older men is less than in men between the ages of twenty and forty but the amount in cases of carcinoma of the prostate does not differ from that in control cases of a similar age group. There also is no significant difference in the relative amounts of alpha and beta fractions present in the patients with and without carcinoma of the prostate. The patients with carcinoma of the prostate who had been castrated from ten to twenty-four months previously and in whom there had been a recrudescence of the disease, showed no difference in 17 ketosteroid excretion from that in the untreated cases. JOHN A. LOFF, M.D.

Donahue, C. D.: The Use of Stilbestrol in Carcinoma of the Prostate. *Northwest M.* 1944, 43: 284.

At present the use of stilbestrol is rather empiric. Yet there is a fairly sound basis that justifies its employment. The interrelationship of the pituitary, thyroid, adrenal, prostate, and testicular glands is common knowledge. If there is an imbalance created in this interrelationship tissue growth is thrown out of balance.

Orchiectomy has definitely proved its value in malignant growths of the prostate, yet there are instances in which no improvement was noted. This is in part explained by Herbert's autopsy reports, in which he cited enlargement of the adrenal glands to four and seven times the normal size. This occurred in 1 patient who failed to respond to castration. Undoubtedly the pituitary gland was playing an important part in androgen control. It is the

author's belief that variability in response to the castration method may be explained by the close interrelationship between the endocrine functions.

He does not think that stilbestrol has been given a fair trial by some, especially when he reads that 1-mgm. doses by mouth have been given with unsatisfactory results.

More than 40 cases are under treatment at the present time. In consideration of the dosage the author has become more bold and followed the course of others in administering 40 intragluteal injections 3 mgm. each a total of 200 mgm. and then a maintenance dose of 1 mgm. each night on retiring. Patients are required to call at irregular intervals for recheck and repeat with a second course if necessary.

The largest total dosage was 1,440 mgm. given over a three and-one half year period. There has been no unfavorable reaction.

As far as maintenance dosage is concerned the author is not certain that 1 mgm. doses are sufficient.

As to toxic effects only 1 case seemed to be definitely reacting to stilbestrol with nausea and vomiting, which prompted the discontinuance of the treatment. Other side-effects were minor namely swollen breasts and sore nipples.

JOHN A. LOFF, M.D.

Marshall, V. F. Subtotal Perineal Prostatectomy: Presentation of a New Technique. *J. U. A. Balt.* 1944, 52: 250.

The perineal approach for prostatectomy is an established urological procedure.

Four advantages of subtotal perineal prostatectomy i.e. the removal of almost all or all of the capsule but with retention of most of the bladder neck, over perineal intracapsular enucleation seem noteworthy.

1. An unrecognized carcinoma may be removed.
2. Many fibrotic infected or stone-bearing prostates are best treated by this procedure.
3. Hemorrhage is well controlled under vision.
4. Subsequent urinary control compares favorably with that following other methods.

The approach for subtotal perineal prostatectomy follows Young's classical description and need not be described here. Occasionally Belt's modification is used but the exposure is not quite so good.

After the rectal surface of the prostate is exposed, biopsies are taken from any suspicious areas and frozen sections made. If carcinoma is present Young's radical operation is done. The fascia overlying the seminal vesicles and ampullae is incised transversally and the lower portions of these organs are well exposed. These lower portions may now be divided distal to right angle clamps (so-called gall bladder clamps) and the stumps transfixed with 0 chromic catgut, but it is usually easier to do this later. When desired the vesicles and ampullae may be dissected free and removed *in toto*. Then the tissues on the sides of the prostate are pushed upward by blunt dissection with the handle of the scalpel so that all loose tissue is crowded into the

region of the anterior commissure. An incision is next made two-thirds of the way around the lower circumference of the urethra at the junction of the apex of the prostate and membranous urethra care being taken to avoid the external sphincter region. When necessary a cystoscope can now be passed for examination of the bladder. One blade of a heavy curved scissors is inserted into the urethra and placed in the groove between the upper part of the lateral lobe and the anterior commissure. The other blade is in a corresponding position outside of the whole thickness of prostate superiorly and in the space previously created by blunt dissection. An incision is now made back to the muscle of the bladder neck and the step repeated on the other side. By palpation the more or less vertical groove on either side between the lateral lobes and the bladder on the interior of the bladder outlet is found and with the scissors the upper halves of the lateral lobes are excised from the bladder. A few bleeding vessels are usually found on the cut surface of the bladder muscle and these are clamped and ligated with 00 plain catgut. Prostatic lobe forceps are applied to the lateral lobes, occasionally only one at a time to allow more room. The lobes are pulled downward and rotated laterally, the prostatic urethra being spread open to give a clear view into the bladder and of the remaining sites to be divided. The incision between the lateral lobes and the bladder is continued downward almost to the trigone, any bleeding vessels being ligated in course. The whole prostate is turned sharply downward and traction applied this provides a complete view of the trigone. If the middle lobe is up under the trigone, an incision with the scalpel is made across the apex of the trigone and down to the prostatic tissue, the middle lobe is enucleated from its connections with the bladder and the flap of the trigone raised bluntly which exposes the vesicles ampullae, and chief vascular supply of the prostate these are clamped cut, and ligated to remove the prostate. If the gland has not enlarged under the trigone this is usually not necessary and right angle clamps can be applied and the gland removed. The clamped tissue is transfixed with sutures of 0 chromic catgut.

The closure is proceeded with in the following fashion.

Chromic 0 catgut is used for suture material. A mattress suture is placed in the roof of the bladder neck and the roof of the urethra and tied, the strip of mucosa on the anterior commissure being ignored. This approximates the top of the new outlet. A similar suture is placed through the apex of the trigone, including the bladder neck musculature beneath it and into the floor of the urethral stump. This approximates the floor of the new outlet and leaves the excess opening into the bladder on either side. A 30-cc. Foley bag catheter (usually size 22 or 24 French) is inserted through the urethra into the bladder and inflated. The bladder is thoroughly irrigated before complete closure. The openings on either side are now closed transversally with in-

interrupted single sutures through all the layers of the bladder wall. At a suitable point on either side, one of these sutures also passes through the lateral wall of the urethra. Considerable care is taken that the sutures are tied only tightly enough to approximate the tissues so that there will be no necrosis. The closure should be watertight to moderate irrigation and, if not, a few extra sutures may be placed at the required points. The wound is irrigated, and if appreciable infection is expected about 1 gm. of sulfonamide powder is dusted in it. One thin rubber tissue drain is inserted to the suture line. The levator muscles are loosely approximated with interrupted single catgut sutures; the subcutaneous tissue with "o" plain catgut, and the skin with fine silk. The drain is brought out one angle of the wound and sutured to the skin with silk.

JOHN A. LOAR, M.D.

MISCELLANEOUS

Haller, C. G. and Myers, G. B.: The Male Climacteric; Its Symptomatology, Diagnosis, and Treatment. *J. Am. Med. Ass.* 944, 126-172.

The authors point out the subjective similarity of the male climacteric, psychoneurosis and psychogenic impotence. Because of this fact it is undertaken to distinguish these conditions by laboratory tests and to determine if the male climacteric is a normal accompaniment of the aging process or a pathological condition. Further, the therapeutic value of hormones is investigated.

Since it is known that in the female the menopause is accompanied by an elevation of the gonadotropin titer an investigation was undertaken to show whether or not such elevation is a true index of testicular failure.

Twenty-five normal men in the age group from the third to the tenth decade were subjected to the gonadotropic content of twelve hour night urine. The ovarian weights of the injected white rats averaged 12.3 mgm., which finding was similar to that in the injected control rats.

In the cases of 12 castrated men the ovarian weight was increased fivefold (58 mgm.) which is to be interpreted as testicular failure. The urinary gonadotropic elevation was further revealed in 8 prepubertal castrates. Again the gonadotropin increase was revealed in 20 cases by hyalinization of the seminiferous tubules and clumping of the Leydig cells.

Urinary gonadotropic assays in 38 men complaining of symptoms similar to the female menopause demonstrated two distinct categories: (1) 15 patients with normal gonadotropic assays, and (2) 23 individuals in which the hormone was decidedly elevated, which suggested a lack of testicular function and this was confirmed by histological examination of biopsy specimens in 8 individuals.

Testosterone propionate was exhibited in 20 of these patients, 9 of group 1 and 10 of group 2. The 20 patients in the last group were subjectively im-

proved in one week, and 17 were completely relieved at the end of three weeks but the remaining 3 continued to have psychic and constitutional symptoms in spite of therapy for several months after which vasomotor and urinary symptoms were abolished. In 2 cases the loss of sexual vigor was refractory to therapy until 50 mgm. of testosterone propionate was given five times weekly. In 14 cases the therapy was withheld and all symptoms including sexual impotency returned, and this was again reversed by the exhibition of testosterone propionate. None of the patients demonstrated improvement when placebos were substituted for the hormone without the patient's knowledge. The subjective improvement, followed by return to the original symptoms, failure of the placebos to afford subjective relief, and, finally improvement with re-establishment of therapy are demonstrated by the concomitant curve of urinary gonadotropic assays.

In reviewing the symptomatology the authors noted similar symptoms in the groups except that in the former group there were distinct hot flashes while in the latter the symptoms were present more or less, throughout life with the onset following psychic trauma.

It was concluded that the male climacteric may occur as early as the third decade (1 case reported was that of a twenty-five-year-old man) but it is a relatively rare syndrome, probably affecting only a small proportion of men who live into old age, and therefore, distinctly a pathological process.

Androgen therapy is contraindicated in (1) the presence of carcinoma any place in the body (2) the presence of edema since androgen tends to produce sodium and thus water retention and (3) the presence of normal testes, since testosterone inhibits spermatogenesis and disuse atrophy of the Leydig cells.

The authors advise a therapeutic test for the male climacteric in instances in which laboratory facilities are not available. Testosterone propionate (35 mgm.) is given intramuscularly five days weekly for two weeks. If there is no subjective improvement or a return of sexual potency two conclusions are permissible: (1) that the patient does not have the male climacteric, or (2) that excessive dosage of testosterone is necessary which makes the therapy impractical. On the other hand, if the patient responds it is then essential to determine if he is suffering from testicular inadequacy and this is accomplished by discontinuation of the therapy with a return of symptoms symptomatic continuation with placebos and finally further androgen treatment with relief of the symptoms again.

It was the finding of the authors that complete testicular failure can be usually controlled with 25 mgm. of testosterone propionate given thrice weekly in some cases given once weekly and rarely with 10 mgm. given once or twice weekly. Implantation of pellets is advocated in instances in which two or more intramuscular injections of testosterone propionate are necessary weekly. From 4 to 8 pellets

are implanted subcutaneously in the thighs and provide control for periods of from six to ten months. Methyl testosterone has been found to be disappointing as a means of replacement therapy and moreover it is toxic in large doses.

ROBERT LICH, JR. M.D.

Trattner H. R., and Walzak, B. J.: Studies Concerning Effects of Calcium on the Urinary Tract. *J Urol* Balt. 1944, 52: 357.

Effects following the intravenous injection of 10 cc. of a 10 per cent solution of calcium gluconate on the musculature of the renal pelvis and calyces, ureter and bladder were studied by four different methods in a total of 282 patients.

The injected calcium did not alter spastic states which included spasm of the renal pelvis and calyces in 17 per cent, of the ureter in from 17 to 71 per cent, and of the bladder in 30 per cent of the patients. There was persistence of pain in 30 per cent of the patients having ureteral colic. No notations of urinary pH were recorded.

Excluding instances of slight to moderate relaxation, the injected calcium was found to produce a marked relaxation which overcame a previously existing spastic state in 30 per cent of the renal pelvis and calyces, in 27 per cent of the ureters and in 57 per cent of the bladders. Forty per cent of the patients having ureteral colic experienced complete relief from pain. No notations of urinary pH were recorded.

When relaxation followed calcium injection defects which had appeared in the urogram because of contracted or spastic states disappeared. This finding proved to be of important assistance in urographic interpretation. It was also observed that a greater amount of opaque solution could be tolerated by a patient with minimal or complete absence of pain.

From bladder filling determinations before and after calcium injection it was found that the urinary pH has an important and very definite relation to calcium action in that relaxation of the bladder occurred in a greater degree with and greater frequency on the acid side particularly between pH 5.0 and 6.3 while diminution in capacity of the bladder i.e. increased tone or spasm, took place to a greater extent and with more frequency on the alkaline side. Thus there appears to be an optimal acidity of the urine in which the antispasmodic or relaxing effect of the calcium is more likely to take place.

The injection of calcium for the purpose of relaxation is contraindicated when the urine is alkaline because of decreased effectiveness, negative results or reversal of action. There is less certainty of relaxation when the urine is of high acidity than when it is within the optimal acid range.

The incidence of relaxation should be expected to occur in a greater percentage of cases than is reported in this article if calcium is injected when the urine is in the optimal acid range indicated, or if the patients are properly acidified prior to such administration.

JOHN A. LOEF M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Helfet A. J.: Acute Manifestations of Yaws of the Bones and Joints. *J Bone Surg* 1944, 26 672.

In the tropics yaws is the most common bone and joint disease. It is very often associated with tropical ulcers and cracked, painful skin especially on the feet. The manifestations of yaws are so similar to syphilis that differentiation often becomes very difficult. It is said that yaws does not affect the viscera and the central nervous system. The symptoms of syphilis are characterized by bone pain especially at night and when the limb is warm and dependent. This is associated with the picture of bone sclerosis. Patients affected with yaws present a more rapid and painful picture.

The history is rarely older than a few weeks and already definite, characteristic features are seen on the roentgenogram. There are single or multiple "punched out" areas, subperiosteal necrosis of bone with raising of the periosteum and deposition of new bone which often takes the shape of onion-layer.

Yaws near joints may simulate arthritis, as it causes pain, swelling, muscle spasm, and limitation of motion. Syphilitic gummatous lesions rarely show these clinical manifestations. Yaws in the shaft of long bones frequently resembles septic osteomyelitis. The disease is found in any part of the skeleton. The tibia, lower end of the femur, medial end of the clavicle and lower end of the humerus are predominantly involved. The Wassermann and Kahn reactions are always positive.

The microscopic picture of yaws is very similar to that in syphilitic lesions with the exception that endarteritis obliterans—which is so characteristic in syphilis—is absent in yaws. The joints and tendon sheaths are very often affected by this disease. In joints yaws produces a painless chronic synovitis. Articular cartilage is not affected. When the tendons are affected the formation of ganglia or tenosynovitis is very common.

Arsenicals are used in antiyaws treatment. The author used acetylsalicylic acid or novarsenobillon (N.A.B.) or alternate doses of bismuth and sulfostab. Under this treatment subjective complaints disappear readily. The objective findings, however, subside very slowly.

The author states that his investigations on yaws in Africans in Africa were hampered by two facts. The African has little appreciation of time, and therefore, the past and present history was unreliable. Also he is very often affected by a multiplicity of diseases which obscure the clinical picture considerably. The most common diseases were chronic malaria, dysentery (entamoeba histolytica) and bilharziasis.

GEORGE I. REISS, M.D.

Boyd H. B.: Congenital Talonavicular Synostosis. *J Bone Surg* 1944, 6 682.

The author reports 4 additional cases of talonavicular synostosis, a condition previously described as being unusual and very rare.

A white girl of ten years, a white boy of ten years, the boy's father aged forty five, and the boy's grandmother aged seventy-two—all presented talonavicular synostosis. They had very little or no complaints.

The author points out that the relationships of the last 3 patients suggest a hereditary nature of the condition.

A number of x ray reproductions show the fusion of the talus and the navicular bone very distinctly.

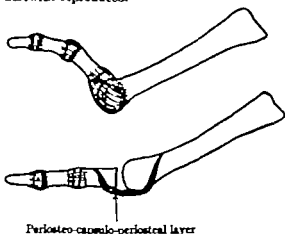
GEORGE I. REISS, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

King, B. H.: Lantzon's Periosteocapsuloplasty for Congenital Dorsal Subluxation or Congenital Overlap of the Fifth Toe. *South. M. J.* 1944, 37 614.

Simple amputation of the fifth toe for congenital overlap or subluxation has not eradicated the pressure symptoms about the plantarolateral aspect of the fifth metatarsal head which recur postoperatively. A new technique is herewith reported. Eighteen such fifth toes have been corrected by an operation called periosteocapsuloplasty (Lantzon's) in 11 soldiers with satisfactory results. All of the patients complained that the involved fifth toe rubbed on their shoes and uniformly exhibited dorsal clavi.

The operative procedure is described in detail and is accompanied by two diagrams, one of which is herewith reproduced.



Periosteocapsuloplasty

Fig. 1. a, top, Diagrams lateral view of fifth toe and metatarsal before operation. b Diagrams lateral view of correction obtained by operation.

After the fifth metatarsophalangeal joint is exposed, the extensor digitorum longus tendon is cut from its distal insertion and transplanted onto the fifth metatarsal neck. The dorsal periosteocapsulopostotal layer covering the fifth metatarsophalangeal joint is reflected mediolaterally. This in addition to the tendon transplantation, augments release of the "bow string" with complete reduction of the existing subluxation deformity. A mattress suture of the reflected capsulopostotal layer introduced under the metatarsophalangeal joint not only reverses the "bow string" but maintains it. When this suture is tied no intervening tissue remains between the bony structures and the skin. The redundant capsular element is now transfixed under the fifth metatarsophalangeal joint. The skin is closed in the usual manner. Copious dressing and adhesive are the only immobilization used. The author recommends weightbearing three weeks postoperatively.

SAMUEL L. GOVERNALL, M.D.

FRACTURES AND DISLOCATIONS

Allende, G., and Freytes, M: Old Dislocation of the Elbow. *J Bone Surg.*, 1944, 26 691

During the past ten years the authors have treated 35 patients with old dislocations of the elbow who presented themselves for consultation from twenty days to five months after their injuries. If a dislocation is not reduced immediately osseous and fibrous changes occur around and in the elbow joint which make manual reduction impossible.

Fractures were associated with the dislocation in 13 of the cases in this series. Fracture of the medial epicondyle in 8 cases, of the tip of the coronoid process in 3 cases, of the lateral epicondyle in 1 case, and of the lateral condyle in 1 case. Fracture of the head of the radius has never been found in old dislocations.

Ossification of the posterior and anterior aspect of the inferior extremity of the humerus scar formation in the olecranon fossa, and shortening of the triceps were the outstanding pathological changes observed in these elbow joints.

Operative reduction of the dislocations was performed in all cases. The patient was placed face down on the table, and an incision was made on the posterior aspect of the elbow joint. The shape and size of the incision varied. The ulnar nerve was located, freed and retracted. The triceps was severed following an inverted U line. The ends were retracted proximally and distally and to both sides until the radius became visible laterally and the humerus became visible medially. The joint was opened by flexing the arm. Fibrous tissue and ossification were removed. The ends of the triceps muscle were sutured with catgut or No. 34 stainless steel wire. The ulnar nerve was replaced. The skin was sutured. A plaster-of-Paris cast was applied from the axilla to the metacarpophalangeal joints the elbow being kept at an angle of 130 degrees in the cases with stable reduction and at an angle of 90

degrees in cases in which a tendency toward redislocation was noted.

In from eight to ten days after the operation the cast was opened. Exercises and hot salt baths were given and the arm was replaced into the cast after each treatment. This was done for a period of one month.

Functional results are described as being satisfactory. The elbow was painless and stable with a range of movement that varied between 40 and 120 degrees in the various patients discussed.

Other methods of treatment of old dislocation of the elbow were discussed. Farabeuf recommended in dislocations less than four or five months old, the use of strong traction by flexing and extending the arm and then pronating and supinating it with the object of breaking down adhesions and facilitating later manipulative reduction. Watson Jones recommended in some cases the use of Thomas's sham reduction which consists in flexing the elbow at a right angle and keeping it so in a sling for three weeks after which the patient forms a nearthrosis by active movement. Arthroplasty was very successful in the hands of Putti and Serra.

The authors finally discuss the indications for 3 surgical approaches: the posterolateral approach of Kocher, the transelecranal approach in which vital hum screws are used to approximate the separated fragments and the transtendinous approach.

GEORGE I. KRIS, M.D.

Ponassi I: Causes of Failure in the Treatment of Congenital Dislocation of the Hip. *J Bone Surg* 1944, 26 775

A study has been made of 120 patients with congenital dislocation of the hip with the object of determining the causes of failure in the treatment of this condition.

The cases were divided into the following three groups:

Prenatal dislocations in which the dislocation is present at birth.

Postnatal dislocations in which the patient presents a predislocation at birth which slowly pro-



Fig. 1. Abduction bar applied.



Fig. 2. a, left, Outward rotation of the foot is locked at 75 degrees. b, There is free inward rotation.



Fig. 3. With the abduction splint applied, the femoral heads are centrally situated in the acetabulum.

gresses during the first year of life until it becomes a well established dislocation when the patient begins to walk. The 'bifidation' of the acetabular roof shown on the roentgenogram is characteristic of most of these cases.

Doubtful cases in which both the primary and secondary acetabula are well developed but in which the roentgenogram shows them to be separated by a bony ridge. In these cases it was impossible to determine how and when the dislocation took place.

Treatment in the prenatal cases generally resulted in failure. Putti's abduction splint is indicated only during the predislocation stage of the postnatal dislocations.

The anteversion of the femoral neck plays an important role in the maldevelopment of the hip after immobilization.

Except for the prenatal dislocations and a few dubious and postnatal cases which could not be reduced, the greatest number of failures in the treatment of congenital dislocation of the hip is to be found

1. In epiphysitis of the femoral head

2. When there is a tendency of the head to become subluxated, which occurs at the beginning of the walking exercises

3. In osteoclerosis of the acetabular roof

If better results are to be obtained in the treatment of congenital dislocated hips we shall have to direct our efforts to diminishing the incidence of epiphysitis and to establishing a careful and prolonged after treatment to favor the development of the acetabular roof. It was noted how frequently cystic atrophy of the femoral epiphysis occurs, and that a flattened head results in 50 per cent of these cases. The cystic atrophy starts to develop from the fifth to the seventh month of immobilization, and progresses until the removal of the cast. The longer the immobilization, the greater and more frequent is the cystic atrophy. As has been mentioned, the author believes this lesion to be related to the poor biological condition of the primary acetabulum, where the femoral head is placed after reduction. The best conditions for the head will be provided by an early development of the new hip joint with all its components but mainly the development of the

synovial lining. In a baby a good part of the femoral head is cartilaginous and we know how much the nutrition of the cartilage depends upon the synovial fluid.

It seems logical that a joint, which is the main organ of motion will develop better with motion than with rest. The retention of the head in the primary acetabulum should be the principal aim of treatment during the first months after reduction. As soon as the danger of redislocation has disappeared, the rebuilding of the new hip joint will be better accomplished by the establishment of controlled motion.

From the study of this series it has been learned that the persistence of the Trendelenburg sign for more than two or three months after the patient has begun to walk indicates a poor prognosis. If the gait does not recover and a positive Trendelenburg sign persists the femoral head is subluxated on each step because of the tilting of the pelvis, and the reconstruction of a good acetabular roof becomes impossible.

It has been said by different authors, and mainly by Krida and Badgley in this country that one of the main causes of dislocation is the anteversion of the femoral head. Because of this anteversion it is necessary that the leg be maintained in inward rotation to obtain centralization of the femoral head in the acetabulum and outward rotation should be avoided for a long period after treatment. The best way to accomplish this would be to strengthen the inward rotators of the hip which have been weakened during the period of immobilization.

The authors believe the postreduction treatment of the congenitally dislocated hip should be directed as follows

1. Functional treatment should be started as early as possible to avoid or diminish epiphysitis of the reduced hip.

2. Prolonged controlled, functional treatment with the legs in abduction, should be carried out in order to secure the central position of the femoral head in the acetabulum, and to make possible a good development of the acetabular roof. Outward rotation of the legs should be avoided, but free inward rotation should be allowed in order to stimulate the development of the inward rotators.

One year ago the authors began to treat a group of congenitally dislocated hips in the following way:

1. The reduction of the hip is done following Reddon's technique—the method which has been used in the State University of Iowa Hospitals for many years.

2. A well molded, bilateral plaster hip spica is applied with the hip in 90 degrees of flexion and from 60 to 70 degrees of abduction in both unilateral and bilateral dislocations. This position is recommended by Waldenstrom in order to avoid overstrain on the adductors which "press the femoral head with great force against the acetabulum and the anterior part of the capsule. If the reduction is stable the knee joints can be left free. If the head redislocates easily the plaster cast must be extended below the knees. This position is maintained for from three to four months and then under anesthesia the legs are brought to Lange's position with as much inward rotation as possible. A bilateral long leg hip spica is applied for two additional months.

3. Following the five or six months of immobilization, the controlled functional treatment is begun. With the object of (a) keeping the legs in abduction, (b) avoiding the outward rotation of the legs and (c) giving them free motion in other directions an abduction bar was devised. This splint consists of an iron bar with a plate inserted on each end. The plates which are attached to the heels of the baby's shoes, have free inward rotation, while the outward rotation is locked at 75 degrees. The distance between these two plates can be controlled by sliding the two pieces which form the bar. The legs should form an angle of 100 to 120 degrees.

This abduction bar is kept on the patient continuously except for the daily bath, from two to six months following removal of the cast. At the end of two to six months according to the development of the hip joint the child is allowed to walk for two hours daily for the next month. The splint remains applied for the rest of the day. The length of time the patient can walk each day can be determined from successive roentgenograms but probably during the first year after reduction daily walking should not exceed from two to six hours. The splint must be applied at night for at least three years following reduction, even if the roentgenogram shows a well developed hip. We are dealing with a congenital deformity which has a strong tendency to persist.

The author's observations on open reduction and shelf operations are as follows:

Open operation proved to be useful in several of the older cases in which an hour glass constriction of the capsule, a too-long round ligament, or adhesions of the capsule to the wall of the iliac bone were the causes of the irreducibility. The hour glass constrictions and the adhesions of the capsule were late sequelae of old congenital dislocations. In no patient under four years of age were such conditions found and consequently the author concludes that open operation is rarely indicated in young children.

The shelf operation was successful only in the cases in which the femoral head could be well placed in the center of the acetabulum. The shelf with the head above the primary acetabulum gave a poor functional result.

ROBERT P. MONTGOMERY, M.D.

Savini, C.: Ambulatory Treatment of Fractures of the Lower Extremities. *Am J Surg* 1944, 66: 44.

In the ambulatory treatment of fractures of the lower extremities after the fracture has been reduced and the limb immobilized the patient should be allowed to leave the bed as soon as possible. Getting out of bed is the first and most important part of the treatment. Walking is of secondary importance, and should be left for a later time and mostly to the discretion of the patient.

To be out of bed insures better nutrition, better digestion, a better general condition and, as a consequence, better healing of the fracture.

Patients should not be urged to walk too soon. Generally they are too eager to walk. However once they have acquired confidence, without any instruction, encouragement or assistance they generally move around and walk within a very short time.

An ambulatory treatment is seldom possible when the fracture was treated with open reduction.

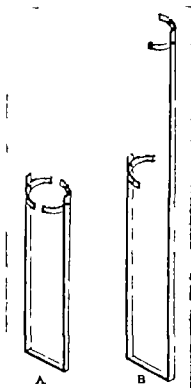


Fig. 1. Models of stirrups. A, for fracture of leg; B for fracture of hip joint. Each stirrup is made with duraluminum $\frac{1}{4}$ inch wide and $\frac{1}{8}$ inch thick. Two plates of pliable metal are attached to the top branches of the stirrup serving to hold the stirrup on the ring of the bandage covering the leg. The bases of the stirrups touching the ground are covered with rubber.



Fig. 2. Apparatus for fracture of hip complete eight 5 pounds. Plaster of Paris bandage was removed from the leg to permit massage (Courtesy of American Journal of Surgery.)

but it was very successful when fractures were treated manually and required only a light plaster of Paris bandage to keep the fragments in place.

From January 1 1933 to December 31 1943, 148 of a total of 232 cases of fractures of the lower limbs referred to the author's care were treated ambulatorily: 10 fractures of the neck of femur, 5 fractures of the patella, 23 fractures of the tibia and fibula, 20 fractures of the tibia, 16 fractures of the fibula, 49 fractures of the malleoli, and 25 fractures of bones of the foot.

All these patients were treated as emergency cases, and the fracture reduced immediately or as soon as possible after their admission to the hospital. A plaster-of-Paris bandage and a metal stirrup were applied at the same time. Patients with fracture of the leg were generally out of bed the next day after admission, some of them a few days later and on the average were discharged from the hospital in one month.

In the treatment of fractures of the leg and foot, after reduction the fractured leg is immobilized and at the level of the tuberosity of the tibia, a length of plaster-of-Paris bandage is applied sideways and rolled around the leg to form a 1 inch wide and 1 inch thick ring as a part of the plaster-of-Paris covering the leg, to serve as a good support to the metal stirrup. The stirrup is longer than the leg so that when the patient is standing, it rests on the

floor the foot remaining suspended and not touching the floor. Thus walking is made easy and there is no danger of traumatic flat foot.

For fractures of the hip joint, the treatment is as follows:

Following reduction and after a light bandage of plaster-of-Paris has been applied on the whole limb, another stirrup is used: the external branch of which is made long enough to measure the distance from a little below the crest of the iliac bone to the floor and its internal branch to reach the middle part of the thigh of the patient. To support the stirrup, the plaster-of-Paris bandage covering the entire limb is reinforced with two rings, one just below the crest of the iliac bone, circling the lower part of the abdomen and the other at the middle part of the thigh. When the stirrup is applied its base rests on the floor and the foot remains suspended.

The stirrups can be made of duraluminum; they are then smaller and lighter in weight; they are kept fixed to the limb with plaster-of-Paris bandages, day and night.

Only a few plaster-of-Paris bandages should be used in order that the resulting cast be very light and thin. To insure immobilization, we must trust more to the stirrup than to the thickness of the bandage.

A complete apparatus with stirrup for immobilization should not weigh more than 5 pounds for a fracture of the femur and not more than 3 pounds for a leg fracture. ROBERT P. MORREHEAD, M.D.

Bernstein, A., and Stone, J. R.: March Fracture. A Report of 307 Cases and a New Method of Treatment. *J Bone Surg* 1944, 26: 744.

From this series of 307 cases of march fracture the following conclusions were drawn:

Prior to the introduction of "speed hikes" and prolonged marches in the curriculum of basic training, march fractures were rare entities. Soon after this change in the curriculum occurred, this syndrome was seen.

This pathological condition occurred in soldiers irrespective of age, height, weight, and general body build.

No usual or unusual deformities of the foot are associated with this condition.

One or more of the metatarsals may be involved at the same time, or at different times during the same training cycle.

There is no relation between preduction occupation and the development of a march fracture.

Contrary to general opinion, this condition occurs in the colored soldier although not nearly so frequently as in the white soldier.

The treatment, as described in this article, was found to be adequate enough to keep the soldier on duty without missing the greater portion of his training. After six or eight weeks, the soldier is able to perform his duties as well as the man who never had a march fracture.

The method of treatment described saves innumerable hospital and training days.

In the authors' opinion the treatment of a march fracture of the foot by immobilization in a plaster of Paris bandage, as described in the literature is not indicated since this is not a complete fracture and there is no loss of position or alignment. Furthermore rigid immobilization causes bone and muscle atrophy of the involved foot and leg. When the plaster cast has been removed it is necessary for the patient to receive physical therapy over a period of several weeks before he can return to his normal duties. With the new method of treatment all this is obviated.

The treatment is not original but has been used previously for fractures of the toes, bursitis between the heads of the metatarsals and various other conditions of the foot.

Patients with a march fracture complain of pain during the push-off phase of the gait, that is when the weight is born on the heads of the first, second, and fifth metatarsals with the toes dorsiflexed and the heel off the ground. If during the gait the foot is held rigid thus eliminating motion at the metatarsophalangeal joints the pain is markedly decreased. In order to accomplish this same rigidity a steel bar from $\frac{1}{2}$ to $\frac{3}{4}$ of an inch wide $\frac{3}{8}$ inch thick and 6 inches long is countersunk into the sole of the shoe. Originally this bar was countersunk on the weight bearing surface of the sole but as the sole wore down the metal became more prominent acted as a rocker and caused discomfort. At present the steel bar is countersunk on the underside or non weight bearing surface of the sole and is held in position by 4 rivets.

The relief obtained by this means is very definite and becomes more noticeable after several days, that is as soon as the patient becomes accustomed to walking with a stiff soled shoe. In this way the patient may continue the greater part of his basic training with very little handicap. Most patients continue with their full training and are rarely hospitalized.

Occasionally the patient is further relieved by placing a felt pad along the longitudinal arch in order to redistribute the weight. The steel bar is kept in position for approximately four or five weeks at which time the fracture has solidly healed. The metal bar can then be removed and used again.

Patients with march fracture of one foot are not hospitalized but as soon as diagnosis is made clinically or roentgenographically they are sent to the Camp Shoe Repair Shop, with a requisition for a "march bar." Patients wait for their shoes to be repaired and then report back to their companies for further training. In this way hospital days and training days are saved.

The sooner the bar is applied the sooner can complete recovery be expected. Eleven cases or 3.6 per cent, did not respond to this type of treatment. The latter patients were given thirty-day sick furloughs with instructions to continue weight bearing on the

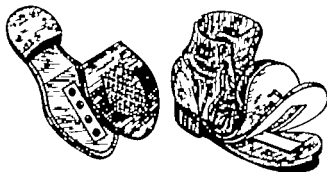


Fig. 1. Showing bar in place on nonweight bearing surface of the sole of the shoe.

injured foot as much as pain would allow. On return from furlough these patients are usually fit for full duty.
ROBERT P. MONTGOMERY, M.D.

Howard J. E., Parsons, W., Eisenberg, H., Stein, K. E., and Reldt, V.: Studies on Fracture Convalescence. Nitrogen Metabolism after Fracture and Skeletal Operations in Healthy Males. *Bull. Johns Hopkins Hosp.* 944, 75, 156.

A study of the metabolism and internal environment of patients who had suffered traumatic skeletal fractures was undertaken with the hope that light might be thrown on the factors which provoke the high incidence of urinary lithiasis and the more rare renal complications with a closer understanding of the metabolic processes during fracture recovery and that therapeutic measures favoring optimal internal and external environment for the recovery of such patients might also be disclosed.

The present report deals with observations on the nitrogen metabolism of 6 patients following fractures of the large bones of the lower extremity and includes comparative studies on 3 patients after operative procedures on the femur and 1 herniorrhaphy. The fracture studies were made on males otherwise healthy whose fractures healed satisfactorily. All patients were at bed rest in casts throughout the entire period of observation. Balance studies were begun as soon as the patients' general condition permitted accurate collections of urine and feces which varied from one to seven days after the trauma had been sustained. In the osteotomy cases it was possible to collect metabolic data preoperatively as well as to make observations immediately after the operation. The results showed that all of the fracture cases showed losses of body protein of considerable magnitude. In 6 patients the average loss of body nitrogen following fracture was more than 220 gm. Expressed in terms of protein, this would be about 1,400 gm. or in terms of normal muscle protoplasm, 15 lb (7 kilos).

The authors have divided their data into two phases: the first of protein loss, the second of protein repletion. On their basis the duration of the phase of nitrogen loss in their patients averaged thirty-five and six tenths days, and the study of their data in the repletion phase shows that these patients re

plenished their lost nitrogen at a very slow rate. Nitrogen losses of a magnitude sustained by their fracture patients are probably of considerable importance to the body economy and must not be overlooked in designing therapeutic measures. The factors which might play a role in these nitrogen losses are disuse anesthesia sulfonamide compound fever and infection they are briefly discussed. Vigorous healthy male patients suffering skeletal fracture treated by ordinary methods sustain large losses of body nitrogen during the early phase of their convalescence. The catabolic nitrogen which is excreted in the urine does not reach its maximum until six days after the injury is sustained and nitrogen equilibrium is not re-established for approximately thirty five days.

Nonfracture operative cases sustain comparatively much smaller and shorter nitrogen losses and repletion is more rapid and vigorous. Disuse atrophy bed rest, anesthesia fever and infection do not account for the major part of the nitrogen losses under discussion. Sulfonamide compounds did not appear to influence the over-all nitrogen metabolism in this group of patients.

EMIL C. ROBITSHEK, M.D.

ORTHOPEDICS IN GENERAL

Ghormley R. K. and Hinchey J. J.: The Use of Aluminum Acetate in the Treatment of Malacic Diseases of Bone. *J Bone Surg* 1944, 26 8

The results obtained by the authors in treatment of malacic diseases of bone with aluminum acetate were as follows:

Of 10 patients suffering from osteoporosis who had followed the treatment six months or more 8 were improved subjectively and 2 were the same as before treatment. All of 8 patients who had Paget's disease and who had followed the program for six months or more were improved symptomatically. In 4 patients who had osteitis fibrosa the condition had improved in 3 and 1 of these had followed the treatment for only two months. The improvement in 2 cases was considerable as demonstrated by

roentgenograms. In the case of 1 patient who had had osteogenesis imperfecta with repeated fractures and deformities since 1914 and who was unable to work and could hardly get around the condition was improved after six months of treatment so that he could get around on crutches and work at a desk. He reported that he felt much better.

The clinical improvement both subjective and objective seems striking enough to the authors to warrant a further trial of the treatment.

The preparation of aluminum acetate used was as follows:

Rx	Solution of aluminum acetate	13v
	Syrup of tolu balsam	15ml
	Honey	to make 32ri

Directions: 1 teaspoonful, three times a day

For children the dose was reduced according to the age and size of the patient.

The use of milk was recommended in all instances, if milk could not be tolerated by the patient, calcium in some other form was used. Vitamin D was administered in all cases.

Ward R.: The Epidemiology of Poliomyelitis. *J Bone Surg* 1944 26 879.

Perhaps the best way to begin a discussion of the epidemiology of poliomyelitis is to state that we do not yet know how poliomyelitis is transmitted.

Studies on the natural history of human poliomyelitis provide no support for the belief in the olfactory portal of entry of the virus, but they suggest that the entire alimentary tract may provide a site or sites of primary attack and invasion. The skin remains a possible portal of entry. The chief mode of elimination of virus at present appears to be by way of the stools. While the striking seasonal incidence the evidence for the human alimentary tract as a portal of entry and the finding of abundant virus in stools sewage and flies, do not establish these latter materials as definite links in the infection chain nevertheless they suggest that poliomyelitis should be placed tentatively in the group of excremental infective diseases until other modes of spread become established.

ROBERT P. MONTGOMERY, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Lange, K., and Boyd, L. J.: Use of the Fluorescein Method in the Establishment of the Diagnosis and Prognosis of Peripheral Vascular Diseases. *Arch. Int. M.* 1944 74 175

Injected intravenously fluorescein can be made visible by a beam of long wave ultraviolet radiation on reaching any area of exposed skin or mucous membranes. A photoelectric method to indicate the arrival of the dye and to measure the intensity of staining may also be used.

In over 1000 patients examined by this method the only untoward reaction was vomiting of short duration during the injection this occurred in 11 patients. Experiments on animals showed extremely low toxicity. The dye diffuses immediately through the capillaries into the interstitial spaces and is partly adsorbed to the plasma proteins. Pathological changes of which do not change the amount of fluorescein immediately available for diffusion. Dead cells do not stain. It has been shown by ultrafiltration experiments that the amount of dye diffusing into the tissue depends on the intracapillary pressure. Changes in capillary permeability alter the amount which diffuses as well as the concentration. Even slight inflammation increases the fluorescence of the tissue. Pigmentation especially in colored people, makes the test unreliable. Determinations of the normal circulation time between the arm and the lip is between fifteen and seventeen and a half seconds, while the time to the legs should not exceed twice this figure.

In 9 patients with acute embolism of the legs it was possible to define exactly the lowest possible level of amputation as far as the skin was concerned, and to decide at once on the probable formation of sufficient collateral circulation to avoid amputation. Block of the sympathetic lumbar ganglions should be performed to avoid mistakes caused by vasospasm. The immediate diagnosis of thrombotic occlusion can also be made. Small gangrenous areas in arteriosclerotic peripheral vascular disease can be judged as to the prospect for healing, localization or further spread varicose ulcers of the leg can be judged as to their outlook for healing and skin grafting, and syphilitic leg ulcers have a specific picture distinguishing them from varicose ulcers. Thromboangiitis obliterans has usually a higher fluorescence than one would expect from the lack of arterial pulsations. Vasospastic disorders have a low fluorescence during the attack, which immediately returns to normal or even increases above normal on blockade of the sympathetic chain. Rubor due to inflammation in a limb with arteriosclerotic peripheral vascular disease can be well differentiated from venous congestion. Thrombophlebitis of the superficial vessels can be well made out as long as it is in

flammatory and the extent of the inflammation can be outlined. WALTER H. NADLER, M.D.

Lazarus, J. A., and Marks, M. S.: Aneurysm of the Renal Artery—True and False—with Special Reference to Preoperative Diagnosis. *J. Urol.*, Balt. 1944, 52: 199.

Aneurysm of the renal artery is a rare clinical entity as evidenced by the fact that the authors were able to collect only 75 cases from the literature. This includes the case here presented.

A history of trauma was elicited in 34.7 per cent of these cases. Among the other etiological factors associated with this condition are systemic debilitating infections and atherosclerosis.

Pathologically aneurysms may be classified as (a) true, and (b) false. True aneurysm is a sacular dilatation of an artery containing all the elements of the arterial wall and results from weakening of the arterial wall as a result of sclerosis, fatty degeneration involving the elastic fibers from some debilitating systemic infection, or from atherosclerosis. A false aneurysm is a sacular dilatation of an artery due to trauma which results in complete disruption of the continuity of the arterial wall either in part or in its entirety in which the limiting walls from without inward consist of adventitia, laminated blood clot and endothelium.

Small aneurysms of the renal artery usually give rise to no symptoms. Larger aneurysms however, usually give rise to symptoms, the most common of which is pain in the loin (62.7 per cent). A mass was felt in the loin in 30 per cent of the recorded cases.

The presence of an opaque ring shadow with a dense periphery on the x-ray film in the region of the renal pelvis is an extremely valuable diagnostic sign of this disease.

The indicated procedure in the treatment of aneurysm of the renal artery is immediate nephrectomy with ligation of the renal artery proximal to the point of origin of the aneurysm.

JOHN J. MALONEY, M.D.

Monahan, D. T.: Ligation of the Aorta and Both Common Iliac Arteries for Aneurysm. *Surgery* 1944, 16: 519.

A forty nine year-old syphilitic negro was laparotomized for aortic aneurysm. The tumor was found to extend from above the inferior mesenteric artery to and involving the bifurcation into the common iliac arteries so that all three of these arteries involved by the aneurysmal sac.

Immediately proximal to the aneurysmal mass, a rubber band about 3/4 inch wide was placed under the aorta and sutured in the shape of a funnel with three No. 1 interrupted silk mattress sutures so placed that if the knots were to slip the sharp stitches would rub on the rubber and not on the aorta itself.

This band interrupted about three-fourths of the circulation into the aneurysm.

Three weeks later the abdomen was again opened. The aneurysm was about the same size and pulsating, although not as strongly as before the partial occlusion. A curved clamp was inserted under the aorta just proximal to the aneurysm and a piece of rubber band $\frac{1}{8}$ inch wide was brought under it below the first band and sutured with 3 fine silk sutures so that the vessel was completely occluded. There was no palpation then of either the aneurysm or the common iliac vessels.

Again somewhat more than a month later the abdomen was opened the area of the second rubber band was exposed, a curved clamp was placed behind the aorta at this site, and 2 heavy silk ties were placed but not tied. At this point brisk bleeding was encountered, the source of which was a tear in the inferior mesenteric artery about $1\frac{1}{2}$ inches from its point of entry into the aneurysm. This vessel was clamped and tied as were also both common iliac arteries about 1 inch from the aneurysm. The heavy silk ties proximal to the aneurysm were then tied. The patient had a relatively uneventful recovery and convalescence. For three months after the last operation the patient complained of pains in the right leg and foot but he was always able to be up and about. These pains were obviously due to the fact that the right leg was not so well supplied with collaterals as the left. Sudden death then occurred from bleeding into the third portion of the duodenum from a perforation of the aorta immediately above the area of occlusion.

Autopsy disclosed that the area of occlusion of the aorta had been transformed into a cicatricial band of cartilaginous consistency and the aneurysm itself and the arterial branches leading away from it had shrunken and filled with old organized clot. The epigastric vessels were competent but not dilated. There were many small vessels which could be seen coursing over the pelvic peritoneum. There was no evidence of a diminished blood supply to the sigmoid colon. Immediately above the occluded area of the aorta there had developed a small secondary aneurysm, with perforation into the duodenum. Syphilitic aortitis was demonstrated microscopically.

The 7 successful (in Bigger's sense) occlusion operations for aortic aneurysm, all reported since 1930, are also briefly discussed. The author arrives at the conclusion that in the region of the lower abdominal aorta at least an occlusion in stages is distinctly feasible and that it would seem likely that from the standpoint of circulatory efficiency many older patients also could withstand total occlusion in stages.

JOSE W. BARROGAN M.D.

Castillo, G. R.: A Contribution to the Forms of Arteritis (Contribución al estudio de algunas arteritis). *Boh. Hosp. Caracas*, 1944 43 53

This is a monograph on the general subject of arteritis wherein the writer quotes, frequently at some length, from current articles and texts by such

authors as Buerger, Edgar V. Allen of the Mayo Clinic, Samuel Silbert and his collaborators, Loz, Magidday, Galloway and Finlay on diabetic gangrene, the lecturers at the 1936 meeting of the Société Internationale de Chirurgie (Vol. II) E. Forgue in the *Precis de Pathologie Externe* for 1939 (Tome I) and numerous Spanish authors as well as Deas, Lewis and Raynaud whose experience and study in this field have led to the acceptance of their expressions of opinion and their published data as medical axioms.

Of course the author does not accede unequivocally to every pronouncement of every authority. Thus, he does not subscribe on the basis of his own material to the pronouncements of Buerger with regard to the etiological influence of race in thromboangiitis obliterans and he is unable to find evidence in Venezuela of any etiological factor in (some) diseases of the foot. Also he does not seem enthusiastic about the newer forms of testing for the circulatory supply of the extremities, such as oscilometry and the Babinsky Heitz modification (immersion of the extremity in hot water for ten minutes), the test of Aldrich and MacClure, the histamine-injection test, the test of Moskowlitz with the Esouard bandage, the test of Cosacresco (scratching the skin with a sharp point with failure in circulatory efficiency of the reddening of healthy tissues), the test of ischemia on elevation and other postural tests, and the test of Collens and Walsky (asking the patient about with observance of the time of appearance of symptoms of claudication) and even roentgenography and arteriography. He seems to prefer simple thermometry with perhaps its combined procedures (Cohn's anesthesia rapida, the test of Brown with typhoid vaccine, and Morton and Scott's infiltration of the posterior tibial nerve), both for diagnosis and evaluation of treatment and for determining the level of any eventual amputation. No etiological effects of cold or of humidity are found in Venezuela where extremes in these conditions do not occur.

The climate about Caracas was also investigated with regard to the temperature of the skin. It was found that with a temperature of 23 C. and a humidity of 75 per cent, the average temperature of the skin on the plantar surface of the big toe was 28.9°C. and that of the dorsum of the foot 29.9°C., but with each increase in temperature of 5°C. 1°C. must be added to each of the figures given.

All of the 15 patients in the author's material were treated, time permitting, with hypertonic saline solution and if gangrene appeared and amputation could wait, preliminary ligation of the femoral artery was carried out. When amputation was decided upon, and its level determined on the basis of all available data, an attempt was made to carry out a leisurely technique with preservation of the usefulness of the limb by the formation of a proper stump. For this purpose refrigeration anesthesia as introduced and developed by Frederick M. Allen was used. Finally any antisyphilitic or other specific

treatment, and the injections of 5 per cent hypertonic saline solution were continued after the operation with a view to procuring a healthier stump and more rapid healing. Of course postoperative infection was avoided if possible with careful asepsis sulfonamides and primary closure. One of the arteriosclerotic patients (a female) was successfully treated with injections of folliculin and 2 of the patients with Buerger's disease underwent lumbar sympathectomies.

There was only 1 fatality and that occurred in the patient with the unknown type of infection (this type of case nearly always terminates fatally) who came under treatment in a condition of extreme gravity with the process evolving with great rapidity.

Four of the 6 persons with the arteriosclerotic form of ischemia had amputations and 2 recovered perfectly without operation the success being ascribed in greater part to the efficacy of the injections of hypertonic saline solution. Of the patients with Buerger's disease, 1 was a chance finding at autopsy and had never had any symptoms leading to the recognition of the condition. 2 patients who underwent lumbar sympathectomy and 3 who did not recovered perfectly under persistent injections of hypertonic saline solution and finally the 2 patients with syphilis got well one following treatment with arsenic and bismuth, and the other following the loss of the anterior half of his foot, under specific treatment combined with injections of hypertonic saline solution.

The problem of arteritis has not yet reached a solution many questions remain to be answered from the viewpoints of etiopathogenesis anatomopathology symptomatology and treatment. However students of this subject are continually bringing to light new knowledge for the benefit of these unfortunate patients who suffer so much and who are so full of hope.

JOHN W. BRENNAN, M.D.

Reynolds, J. T. and Jirka, F. J.: Embolic Occlusion of Major Arteries. *Surgery* 1944, 16: 485

Twenty-four patients were diagnosed as having an ischemia due to embolic occlusion in 27 limbs. Of these limbs 9 were not operated upon. In one patient the embolus had moved and in a second it could not be found. Thus there were 16 limbs from which an embolus was removed at operation (13 patients).

Ten of these emboli were removed within eight hours of their occurrence and all of the patients had a satisfactory return of the circulation. Of the remaining 6 emboli 4 were successfully treated (1 after twenty-seven hours) 1 result was doubtful and 1 was a failure.

Twelve of the patients died. All of these had had emboli removed. Seven died within the first few days after the removal of the embolus apparently from cardiac failure, but all had had successful restoration of the peripheral circulation. Death in 4 of the remaining 5 was not related to the heart disease or the embolus and might therefore have

been avoided. However part of the mortality rate in this series is ascribed to the fact that the authors in consonance with the teachings of de Takata, do not favor operation on an ischemic limb when there is no significant prolongation of the venous filling time and the patient can freely use the muscles of the area in which the blood supply has been threatened. As this is usually true in the presence of emboli involving the arteries of the upper extremities and the popliteal artery referral of such cases was not encouraged. In fact in all of the patients with popliteal emboli included in the present series there was evidence of adequate collateral circulation from the start none was subjected to embolectomy and those who later required amputation were those who did not receive proper care (anticoagulants intermittent venous compression and antispasmodics).

The etiological significance of physical exhaustion and changes or disturbances in the heart rate, particularly sudden variations in the intensity of digitalis therapy, is recognized as well as the importance of locating the site of the occlusion with the aid of oscillometric readings when the diagnosis is made. As soon as the diagnosis is established however heparin (5 to 10 cc.) is administered intravenously at once and the patient is rushed to operation. Heparin is also administered for as long as fifteen days after operation in doses sufficient to maintain the clotting time at about fifteen minutes, and in like manner to patients who are not treated operatively. Fifty milligrams of heparin every four hours have been found adequate to keep this level although larger quantities may often be required. (The antagonistic action of digitalis to the heparin may require adjustment of the heparin dosage.) Recently dicumarol has been used to supplement and supplant heparin. Its dosage has been as follows: 300 mgm. the first day, 200 mgm. the second day and 100 mgm. on the succeeding days.

Preoperative sympathetic nerve block and spinal anesthesia for the operation have been abandoned for fear that the relaxed artery may permit the blocking mass to slip farther to the periphery. This also applies in the case of papaverine and other vascular antispasmodics. Although sympathetic block has reportedly given considerable relief of pain the risk of loss of the embolus makes the preoperative administration of narcotics a wise method of securing analgesia. However sympathetic nerve block may be done just before the patient leaves the table and should be repeated daily during the postoperative period. Papaverine is also given postoperatively. Antispasmodics are of course indicated in cases in which operation is not done.

During this postoperative period intermittent venous compression is also used continuously, either by means of the machine specially designed for this purpose, or with a blood pressure cuff which should be inflated to a reading of between 50 and 70 mm. of mercury and that pressure maintained long enough to fill the cutaneous veins and then left off long enough to allow emptying of the vessels. All



Fig. 1. Illustration to emphasize the maneuver used to extract a clot from an artery in which the clot has become wedged into the bifurcation and in which the arteriotomy has been done below the level of the clot. Note that the end of the probe must be above the clot before it is turned and pulled down. Note also that the probe must be turned away from the direction of the major proximal branch.

though the use of refrigeration has been reserved for those extremities which are unquestionably beyond therapy its recent effect on 3 patients has been so encouraging that in the future it may well be extended. The postoperative treatment may be discontinued after a week or ten days when it is apparent that the peripheral pulse has been restored otherwise cessation of the treatment should be gradual. The sympathetic block may be dispensed with after a week. Intermittent venous compression may then be given less intensively. The anticoagulant should be continued the longest. Two or three weeks should be a minimum time.

With regard to the operation itself, although the technique seems to be practically identical with that for the various arterial ligations it is hoped that refinements in the method of extracting the clot may be made in the embolectomies most often required (those in the femoral iliac, and aortic bifurcations). This is nearly always possible by incising the common femoral artery below the inguinal ligament (Fig. 1)

JOHN W. BENDORF, M.D.

McGrath, E. J., and Hermann, L. G.: The Influence of Estrogens on the Peripheral Vasomotor Mechanism. *Ann. Surg.* 1944, 30 607

Raynaud noticed in 1862 that menstruation had no effect on patients with vasospastic attacks but that the attacks of local syncope disappeared completely with pregnancy.

The authors have made an evaluation of the effect of estrogens on experimentally produced peripheral

gangrene in the tail of the albino rat. (The mode of action of estrogens is essentially that of local liberation of acetylcholine.) All unprotected animals developed gangrene of the tail. All protected male rats also developed gangrene of the tail. Only 1 female rat, however of 40 protected with theelin developed gangrene of the tail, and in these the amount of the gangrene was incomparably less than that in the control animals.

The authors report their experience during the past ten years in translating the foregoing experimental studies into clinical therapeutics. They treated 345 patients with di-ovocyclin (Ciba) (from 0.5 to 1.0 mgrm. 3 times weekly for eight weeks). With the larger doses caution must be used in women. The authors report a high percentage of satisfactory results in the treatment of Raynaud's syndrome, thromboangitis obliterans, arteriosclerosis obliterans, acute arterial occlusion, and chronic, long-standing phlebitis. JOSEPH GASTON, M.D.

Scarborough H.: The Effect of Surgical Operation upon Capillary Resistance. *Edinburgh M J* 944, 5 335

The structure, functions, and physiological behavior of the capillaries in man are not easy to investigate. However the capillary resistance, or fragility (the ease or difficulty with which the capillary will rupture when a pressure is applied to them, can be measured with a satisfactory degree of accuracy provided that certain standard conditions are observed. The capillary walls may be subjected to a pressure strain by an increase of pressure within them, or alternatively by a negative pressure (suction) directed through the skin. Upon the latter procedure has been based a method for the accurate determination of capillary resistance. The resistance of the capillary walls to suction is assessed in terms of the least amount of negative pressure (suction) measured in millimeters of mercury that is required to rupture a single capillary in the area under examination. The procedure does not necessarily measure capillary permeability there are at present no experimental data on the relationship of any between capillary resistance and capillary permeability. Moreover the procedure does not necessarily give any information about the resistance of the capillary walls in organs and tissues within the body.

It has previously been recorded that the extravascular suffusion of blood into the body tissues or alimentary tract is immediately followed by a marked but temporary rise in capillary resistance. The increase frequently amounts to over 100 per cent. It is evident within twelve hours after the injection of as little as 4 ml. of blood into a muscle, or the experimental introduction of blood into either the upper or lower end of the alimentary tract. The intramuscular injection of whole blood plasma, reconstituted dehydrated serum, and particularly of concentrated red-cell suspensions, and transfusions of blood and plasma have all been followed by highly significant elevations of capillary resistance.

In this article are reported the results of exploratory capillary resistance determinations made before and after certain surgical procedures. Before signs within three hours of the time that the operation was started and after means approximately twenty four hours after the operation. No statistical treatment of the data is required to support the conclusion that in 23 investigated cases a remarkable increase in capillary resistance followed surgical operation.

In 6 cases of simple fracture determinations of capillary resistance were made within twenty four hours after the fracture and between five and seven days later. No case was operated upon or received blood or plasma transfusions between the time of the two observations on capillary resistance. In all cases the capillary resistance was significantly higher at the first observation than at the second a finding which supports the results described following surgical operations and which shows that similar increases in capillary resistance follow injuries which do not involve the skin surface.

This increase appears to be independent of the age and sex of the patient, of the anesthetic employed and of the nature of the operation performed. No information is provided by this investigation as to the mechanism of this striking phenomenon for which at present no physiological explanation is available.

JOHN E. KIRKPATRICK, M.D.

BLOOD; TRANSFUSION

Pedley F. G.: Hemoglobin Concentration in College Women. *Canad. M. Ass. J.*, 1944, 51: 331.

The hemoglobin concentration of 864 college girls is given. The estimations were made in the photoelectric colorimeter which is believed to give more consistent results than the conventional hemoglobinometers.

In view of the fact that 40 per cent of the girls showed hemoglobin levels of between 14 and 16 gm. per 100 cc. of blood it is suggested that a "good" if not "optimum" level of hemoglobin in women should be set at about 15 gm. per 100 cc.

The significance of small deviations below this level in terms of efficiency and health is not known.

HOWARD A. MCKNIGHT, M.D.

Propp, S., and Schwind, J. L.: Sternal Puncture as a Practical Diagnostic Procedure. *Ann. Int. M.* 1944, 21: 580.

The author considers the sternal marrow puncture an extremely useful and practical procedure in the study of diseases of the blood and in cases in which the possibility of such diseases enters into the differential diagnosis. However it should be used only on definite indications. A sternal puncture should always be made when (1) the diagnosis is in doubt and a disease usually showing a typical myelogram cannot be excluded—for example an agranulocytosis in which there is the possibility of aleukemic leukemia (2) the etiology of the peripheral blood findings

is obscure ("aplastic" anemia or idiopathic anemia) (3) other means of diagnosis short of surgical biopsy have failed. In addition, a sternal puncture may be made to (1) save time if a specific marrow picture is likely to be present (2) obtain information concerning prognosis (3) determine response to treatment, as in a pernicious anemia which does not seem to benefit from liver-extract therapy and (4) determine the type of a stem cell leukemia when this cannot be done with certainty from the peripheral blood.

The needles are of the 18-gauge spinal puncture type with a heavy finger grip and a stylet. They are cut so that the needle portions are 2 1/2 and 1 cm. in length. The two longer needles are used for adults the choice depending upon the build of the individual, and the smallest one is used for infants and children. The shortness of the needles precludes the possibility of accidental perforation into the anterior mediastinum and prevents bending of the shaft of the needle during its insertion. The puncture is made in the midline of the body of the sternum at the level of the third costosternal articulation. This site is easily found even in obese patients, by using the sternal angle which marks the second rib as a reference point. In children it is advisable to do the puncture in the third interspace because in some individuals the first and second sternbrae do not unite until adult life is reached. When properly carried out under local anesthesia sternal puncture is not a very painful procedure. The puncture needle is inserted vertically and the outer table of the sternum is pierced by a rotary movement of the needle under firm pressure. When the needle is firmly fixed in the sternum, the stylet is removed a tuberculin syringe is attached to the needle and aspiration is attempted. If no marrow fluid appears, the stylet is replaced the needle is advanced a little farther and aspiration is again tried. From 0.1 to 0.2 c.c. of marrow fluid is withdrawn.

The most satisfactory portion of the specimen for study is that which enters the needle last and therefore this is used in making the first smears which are stained with Wright's stain.

Sternal puncture cannot be substituted for a complete clinical investigation of the patient. Indeed the more thorough the work-up of the patient, the easier and more valuable is the interpretation of the puncture. Most diseases unfortunately do not show specific changes in the marrow from which a definite diagnosis can be made, but much clinically valuable information can be obtained which is of aid in the differential diagnosis and subsequent handling of the patient. Diagnosis should be made only from specific myelograms and a negative result does not absolutely preclude the presence of a given disease because of the possibility that a representative sample of marrow may not have been secured or atypical variations in the pathological lesions of the disease may be present. Punctures which yield no marrow cells upon aspiration should be followed by a trephine biopsy if the diagnosis can

be reached in no other way and no contraindications are present.

In the authors' series of 140 cases, 65 per cent of the 74 indicated punctures gave information of clinical value, and the diagnosis was made in 16.2 per cent when this was impossible by any other method short of biopsy. JOSEPH K. SARAT, M.D.

Weiss, D., and Haines, K. E.: Burn Trauma Precipitating Acute Leucemia or a Leucemoid Condition. In *J M Sc* 944 203 490.

The authors present an interesting case of a young colored soldier who up to the time of being severely burned was apparently healthy and able to carry out the usual arduous duties of a soldier. On admission to the hospital his blood picture was normal as time progressed his burned areas appeared to be healing satisfactorily but more or less rapidly as recovery seemed certain his blood picture became chaotic and suggested acute leukemia or a leucemoid condition. Weiss and Haines briefly discuss the infectious theories regarding the etiology of leukemia.

The pertinent contribution of this case report is the possible etiology in relation to the burn. Evidence and opinions that trauma is a possible etiological factor in acute leukemia are cited.

J. M. MORA, M.D.

Adams, W. E., Thornton, T. F., Jr., Allen, J. G., and Gonzalez, D. E.: The Danger and Prevention of Citrate Intoxication in Massive Transfusions of Whole Blood. In *Surg* 944 120 656.

The value of blood transfusions in improving and widening the scope of surgery has become more and more appreciated. They are used to prevent and treat shock and anoxia. Another purpose is the improvement or maintenance of blood plasma proteins, a factor of importance in the healing of wounds and a satisfactory postoperative convalescence.

Actual determinations made following some thoracic operations have revealed that 1,500 cc. of blood are an average loss in lobectomy and pneumonectomy while in some instances it is as much as 3,000 cc. Because of this an attempt has been made to replace the blood with an equal amount of whole blood or plasma in order to maintain the circulating blood in a normal state.

Because of warnings against the too liberal use of citrate in large transfusions experiments were planned by the authors to test the influence of various factors which might contribute to the harmful effects of massive transfusions of citrated whole blood. The methods used are described. The effect of sodium citrate on normal dogs was studied in 23 animals. From these experiments the authors concluded that normal dogs tolerate approximately 0.25 gm. of sodium citrate per kilogram of body weight (sufficient to cover 60 per cent of the estimated blood volume with a 0.41 per cent solution) when not injected too rapidly (over a period of twenty minutes or longer).

The influence of calcium gluconate on citrate intoxication in normal dogs was studied in 4 animals. These experiments demonstrate that when locally available is made available, a higher concentration and a larger amount of sodium citrate may be given more rapidly without fatality (1 gm. per kilogram in from twenty to twenty-eight minutes).

Eleven dogs were studied for the effect of autotransfusions with citrated whole blood following hemorrhages of from 20 to 60 per cent of the estimated blood volume. The authors found that normal dogs will tolerate replacement with citrated whole blood after severe shock due to hemorrhage of from 20 to 60 per cent of the estimated blood volume (with sodium citrate to cover from 35 to 60 per cent of the blood volume) when given over a period of from twenty to thirty-five minutes.

Four dogs were studied for the influence of calcium gluconate on autotransfusion with citrated whole blood following hemorrhages of from 26 to 70 per cent of the estimated blood volume. It was noted that a larger blood loss and replacement with a higher concentration of sodium citrate given more rapidly (from three to thirteen minutes) was tolerated when calcium gluconate was administered.

In a study of 11 animals the authors found that bleeding of from 30 to 50 per cent of the estimated blood volume and replacement with a similar amount of physiological saline solution with or without the addition of calcium gluconate, was well tolerated when administered in from three to twenty-five minutes.

Simultaneous bleeding and replacement of blood loss with prepared citrated (0.41 per cent) whole blood were studied, first without the use of calcium gluconate and later with it. Four animals were used in the first group and 8 in the latter. It was concluded that normal dogs tolerate simultaneous bleeding and transfusion of citrated whole blood amounting to as much as from 75 to 125 per cent of the estimated blood volume. When calcium gluconate was added as much as 200 per cent of the estimated blood volume was removed and replaced without fatality.

The authors found that large doses of citrate were necessary to produce harmful effects and that the rate of injection was an important factor. When the rate of injection of sodium citrate alone or as citrated blood was comparable to transfusions of 1,000 cc. of blood per hour in man, as much as 0.24 gm./kgm. of body weight or sufficient citrate for use in 60 per cent of the estimated blood volume, was safely tolerated. If the administration was over a very short period (sufficient citrate for 60 per cent of the estimated blood volume given in from ten to twelve minutes) the action was usually fatal. No untoward effects were noted when physiological saline solution was used after severe hemorrhage. It appeared to make little difference when calcium gluconate was given with the saline solution.

These experiments would seem to indicate that animals in which shock has been produced are able

to tolerate citrated whole blood somewhat less well than animals in which shock is prevented by the administration of citrated whole blood during the bleeding period. The rate of administration should be somewhat slower in the patients in whom severe shock has resulted from massive hemorrhages.

The picture of citrate intoxication was similar regardless of the type of experiment. Alterations in the blood pressure tracings were observed for several minutes prior to a rapid terminal fall. Some change in respiratory activity was usually present before fatal intoxication. Respiratory failure was never observed prior to cardiac failure. Definite tetanic contractions occurred in some of the second group of animals when citrate intoxication occurred. Eye reflexes were very sluggish. The color of the blood was very dark and gas analyses revealed the oxygen to be as low as 3 or 4 volumes per cent. Severe acidosis was observed.

The use of calcium gluconate in preventing or treating citrate intoxication both in normal animals and in those that had had a loss of blood was extremely effective. The abnormal findings described soon returned to normal. The amount of calcium usually employed in animals weighing from 7 to 14 kgm was approximately 4 gm. (20 cc. of a 20 per cent solution) for the replacement of from 60 to 100 per cent of the estimated blood volume.

The authors conclude that massive transfusions of citrated whole blood for the treatment of extreme shock (blood pressure of from 30 to 45 mm. of mercury) produced by hemorrhage of as much as 60 per cent of the estimated blood volume were safely tolerated in dogs when the replacement of the blood loss was made during a period of twenty minutes or longer. When bleeding and transfusions were conducted simultaneously an average of 115 per cent of the estimated blood volume was exchanged during a period of seventy minutes before the animal expired. This would correspond to a transfusion of 7,840 cc. of blood given during the same period of time for a man weighing 70 kgm. When the rate of bleeding and transfusion was less rapid a larger volume was exchanged without reaction. Thus, a larger margin of safety is present even in massive transfusions of citrated whole blood or plasma when the administration is at the maximum rate currently employed in man (1 000 cc. per hour).

HERBERT F. THURSTON, M.D.

RETICULOENDOTHELIAL SYSTEM

Ballay H. A. and Schreiber, S. L.: Delayed Rupture of the Spleen. *Am. J. Surg.*, 1944, 66, 4.

Rupture of the normal spleen has greatly increased in frequency and is not considered the rarity it was formerly thought to be. The literature has recorded consistent increases explaining that they are due to greater industrial activity and greater use of the automobile.

The spleen is involved in 47.6 per cent of all subcutaneous injuries to the abdomen either isolated or

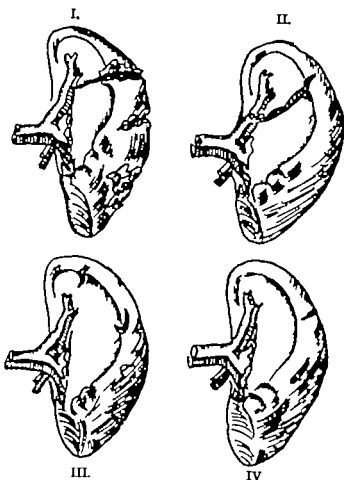


Fig. 1. Top: Diagrammatic representation of types I and II of splenic rupture, both leading to rapidly progressive hemorrhage. Variations of type I are a complete severance of the pedicle and a complete disruption of the spleen. Bottom: Diagrammatic representation of types III and IV of splenic rupture. Type IV is the lesion commonly responsible for the development of a perisplenic hematoma. (From Roettig et al.) (Courtesy of American Journal of Surgery.)

complicated with other injuries. Therefore injury to the spleen outranks trauma to the liver and to the kidney. Yet the diagnosis is too frequently missed. This pertains perhaps mostly to the delayed type of splenic rupture. All too frequently the diagnosis is made at autopsy.

Difficulties in the diagnosis have been described as follows: (1) absent visible signs of injury to the anterior abdominal wall which permits the patient as well as the physician to disregard the early mild symptoms, since the reasoning is that the trauma sufficient to rupture a spleen should cause more visible signs of injury; (2) the history may be misleading, especially in those patients who have had severe or violent muscular activity some hours preceding the onset of symptoms; (3) the shock which is present is thought to result from associated injuries to the head, chest, or extremities or to alcoholism that is the patient may present more obvious symptoms from his associated or complicating

injuries and (4) the recession of symptoms lulls the observers and patient into a false sense of security. Added to these difficulties is the delay of the patient in seeking medical care—that is, the time consumed in getting the patient to the hospital or the doctor to the patient from the onset of the accident—or the time consumed in combating shock so that the symptoms of ruptured spleen may recede or become quiescent—or the difficulty in making the diagnosis in the presence of multiple injuries, which can well explain why a rupture of the spleen can be overlooked.

The authors report a case history of one of their own patients who was suddenly seized with an acute upper abdominal pain and who exhibited a tender right abdomen. X-ray examination was negative. A diagnosis of perforated peptic ulcer was made and at operation a ruptured spleen was found. No history of violence was obtained. Such cases are among the most difficult as regards preoperative diagnosis.

Five types of splenic rupture are described.

Type 1 is a complete fragmentation of the spleen into two or more parts or a complete tearing of the

spleen from its pedicle. This results in a massive hemorrhage and in many instances sudden death.

Type 2 represents a large tear at or near the hilum. This gives rise to grave hemorrhage.

Type 3 is characterized by one large tear or multiple tears about the periphery of the spleen. This type leads to slow and persistent development of the signs of intra-abdominal hemorrhage.

Type 4 is characterized by a solitary tear at the periphery. Symptoms of this type are of recovery after an initial injury and after a period of relief the patient goes suddenly into shock with all the signs and symptoms of a concealed hemorrhage and gradually becomes worse.

Type 5 is a subcapsular hematoma and corresponds to Blocker's Type 2—intrasplenic or subcapsular hematoma. This may be the so-called spontaneous cure group of Wright and Prigot, but, if so, this spontaneous cure is not a fact as no instance of healed splenic hematoma has been found.

The authors present the theories and observations relating to splenic rupture as listed by Zalarski and Harkins.

BENJAMIN GOLDBERG, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Rob. C. G. : The Conservative Treatment of Abdominal Wounds. *Lancet* Lond. 1944, 247 521

This article is based on 141 war wounds with definite abdominal signs. Laparotomy was performed in 98 with 33 deaths. Ten of these laparotomies were found to be unnecessary and 1 of the deaths occurred in this group. Laparotomy was not performed in 43 cases and no deaths occurred among these 43 cases.

In deciding whether or not cases required laparotomy the staff was guided by the patient's general condition, especially his blood pressure and pulse rate. Due allowance was made for the effects of morphine which had been administered previously. Other signs especially considered were tenderness and rigidity, absence of respiratory movements and silence on auscultation.

It was found that the ordinary signs and symptoms of an acute abdomen do not hold in gunshot wounds.

Conservative treatment consisted primarily of observation. Operative treatment was performed in most cases through a paramedian incision. Treatment consisted of suturing all perforations of the alimentary tract proximal to the ileocecal valve. Resection was necessary in 10 cases with 4 deaths. Most of the wounds of the large intestine were exteriorized.

Bladder wounds were sutured and suprapubic cystostomy was performed. Peritoneal drainage was not used in most cases. Wounds of the spleen were treated by splenectomy. Wounds of the liver were sutured or packed. Renal wounds were treated conservatively. Nephrectomy was necessary in 3 cases.

Penicillin and gas-gangrene serum were used prophylactically. Postoperatively blood or plasma, or glucose-saline solution was used. Gastric suction was used when indicated.

The sulfonamides and morphine were used liberally. Blood was administered to most patients postoperatively.

All patients were retained from ten to fourteen days before evacuation.

Residual intraperitoneal abscesses were rarely present. The sulfonamides were given credit for this finding.

Eighteen deaths were ascribed to shock and hemorrhage. 6 were due to peritonitis. 3 patients were beyond visceral repair. Three deaths were due to pulmonary emboli, while cerebral abscess and acute pancreatitis caused 1 death each. In 1 case a high gastric perforation was missed. Six patients died after admission but before they could reach the operating room.

In the cases with recovery the average time between injury and operation was eight and four tenths hours. In those with death from shock, the

average time was fifteen hours. In those with death from peritonitis the average time was twenty five and one-half hours. RICHARD J. BROWNE JR., M.D.

Weddell, J. M. : Surgery in Tunisia. *Brit. M. J.* 1944, 2 459.

The author describes the general lay-out of the medical units with the British forces during the Tunisian campaign and indicates some of the points of interest and lessons learned during that period.

The Thomas splint usually with the metal boot clip was universally and correctly used. Tourniquets were rarely seen and rarely necessary. There was a tendency at times to overdo the injections of morphine. If patients passed through several posts they were sometimes found to have received as much as a grain of morphine by the time they arrived at the operating center.

The question of blood versus plasma has been much discussed. The experience of the British surgeons was that patients with severe injuries could be restored to a reasonable condition with plasma, but that they would not then stand an operation of one hour's duration without blood. Blood was neither wasted nor used excessively. In attempting to forecast the number of patients who will require resuscitation, various factors should be borne in mind. If the unit is dealing with first priority cases, a large proportion (probably over 50 per cent) will require resuscitation. If with second and third priorities there will not be so many. The longer the time lag in the receipt of the cases the more will require resuscitation. Local conditions, cold wet weather, a long journey over rough roads will also have an effect.

Apart from the use of ether for laparotomies and multiple wounds, most patients were anesthetized with pentothal. The advantages of this drug are the rapidity of induction and the freedom from post-anesthetic vomiting—a point of the greatest importance in the busy postoperative wards. Pentothal with oxygen was very satisfactory for the thoracic cases.

In the early stages of the fighting cases were observed from which too much skin had been excised. A few attempts at primary suture, too tight packing of wounds, and insufficient division of the deep fascia were also noted. Adequate division of the deep fascia was found necessary especially in wounds of the buttock, calf and popliteal space.

Extremities and joints. For transport during evacuation some form of the Tobruk plaster was universally used for the lower limb. Generally the limb was encased in plaster with slits for the traction strapping and fixation of the limb to the Thomas splint with plaster bandages. The plasters were always padded and split. For the upper extremity the U plaster from the nape of the neck and including the forearm, was most used and proved satis-

factory The immobilization of extensive soft tissue wounds had been advised, but was perhaps not carried out as often as it might have been. Traction for wounds of the knee joint was occasionally found to have been omitted. The usual faults in plaster work appeared from time to time carrying the plaster beyond the proximal crease of the palm so that stiffness of the metacarpophalangeal joints and fingers resulted. Lack of instruction to the patients to move the fingers and toes continually faulty position of the ankle and foot.

Abdomen The treatment evolved in the Middle East was amply confirmed, suture, when possible rather than resection, exteriorization and colostomy for wounds of the colon and rectum, gastric suction and intravenous therapy as a routine and retention of cases for a minimum of ten days.

Chest Conservative surgery (wound excision and closure of the open pneumothorax) with early aspiration was the rule and proved satisfactory. Great relief of dyspnea was noted after the early aspirations of hemothorax fluid. Many breathless shocked patients were greatly relieved by being propped up, these patients travel better in ambulances and trains when so positioned. The advantage of treating the shock by the completely recumbent position does not compensate for the serious respiratory embarrassment caused. In only a few cases was full thoracotomy indicated in the forward area.

Head At the beginning there was some difference of opinion between the general surgeons and the neurosurgeons as to whether the general surgeons should deal with these cases. It was pointed out that in the forward units the general surgeon had no special equipment for this type of work, diathermy was not available, x-ray examination was not always possible and at the time there was only improvised suction. It was therefore accepted that it was better to get patients back to the neurosurgical unit within forty-eight hours if this was possible, for operation there. The sulfonamides (sulfadiazine when available) were always used.

Burns All coagulation treatment was forbidden as first aid. The routine was sulfanilamide and vaselined-gauze dressing. It was confirmed that cases of severe burns travel badly during the first five or six days after injury.

Chemotherapy Sulfonamides were used prophylactically and therapeutically. To begin with, oral doses at four hour intervals had been advised for all wounded. In practice this broke down on the long lines of communication, and the Middle East sulfanilamide label with the two doses at 8 a.m. and 6 p.m. was adopted. Because of the universal use of these drugs both orally and locally it was impossible to evaluate their effect. The general impression was that they were of value in retarding the onset of infection. Also as compared with the last war the appearance and general condition of the men in the base hospitals seemed better. Sulfanilamide, sulfathiazole and sulfapyridine were the forms mainly in use for surgical cases.

Inacrobic infections Tetanus Up to May, 1943, 1 case of generalized tetanus occurred in a German prisoner of war and 1 case of local tetanus occurred in a British soldier. Both recovered. Gas gangrene: Up to May 1943 there had been less than 100 cases. Treatment consisted of early surgery, large doses of serum, and administration of the sulfonamides.

JOSEPH K. NARAT, M.D.

Morris, G. N.: Experiences with a Mobile Surgical Team on an Amphibious Operation in New Guinea. *Med. J. Australia* 1944, 2, 402.

A surgical team consisting of 3 surgeons and 3 orderlies was detached from a general hospital and assigned to service the troops of an Australian Infantry Division in the battles on the Hoon Peninsula. Its function was to provide surgical treatment for the wounded as far forward as possible. This team worked at the main dressing station of a field ambulance, but never was able to function as far forward as the advanced dressing station. It began service with the initial landing at Red Beach in the attack on Lae. It then leaptfrogged to another point on Lae where it served for ten days, and then moved again to partake in the attack on Finschhafen. In the latter landing, the surgical team began operating within an hour of reaching its site on Scarlet Beach. Most of the time it was found advantageous to dig in the operating tent to a depth of 4 feet so as to protect the patients on the operating tables from flying bomb fragments. On many occasions the surgeons were forced to finish operations in the squatting position.

The total weight of the equipment carried by this 5 man surgical team was reduced to 1,000 lbs. Each was packed in 40-lb. lots. The surgical instruments consisted of 12 hemostats, 2 scissors, 2 tissue forceps, skull forceps, amputation saw, scalpels, needles, and 1 set of retractors, all packed in a kettle sterilized. Also 2 sealed Johnson and Johnson drums containing sterile gowns and dressings, 2 primus stoves and 2 gallons of kerosene were carried. These items approximated a 40 lb. pack. Every man carried just enough clothes for a single change. Only 1 standard light weight portable operating table was carried. Other operating tables were made of crude, forked sticks to which the stretcher was attached. Operating tables were looked upon as a convenience rather than a necessity.

This surgical team treated 400 casualties in a period of three months with a maximum of 50 casualties per day. In this group there were 26 abdominal wounds involving either a solid or hollow viscus, or the mesentery. Many of these were multiple wounds. Other major casualties consisted of 16 penetrating chest wounds, 16 penetrating wounds of the skull, 10 compound fractures of the femur, 22 fractures of the tibia, and 13 fractures of the humerus. The most common wound sites were found to be the arms and legs.

The following points of clinical interest were drawn from these cases:

Patients with head injuries who were completely unconscious from a penetrating wound were not worth operating upon, especially if other serious casualties were waiting for emergency treatment. Further it was not advisable to evacuate penetrating skull wounds for a few days. Patients with penetrating chest wounds should be sutured immediately. Aspiration of a pressure pneumothorax with syringe and needle always proved to be a life-saving procedure. In addition to essential surgery for penetrating abdominal wounds, all casualties in this battle area were given quinine intravenously twice daily to combat malaria. In extensive wounds of the lower extremity, incision for gangrene was delayed until thorough débridement had been made. In 8 cases main-stem arteries were ligated—4 brachial arteries, 1 hypogastric arteries and 3 femoral arteries. In this series, only 2 cases of gas gangrene developed one from a buttock wound and the other from an incomplete débridement. Sodium pentothal given intravenously was the anesthetic of choice. Blood for resuscitation was obtained from combat soldiers of O(IV) blood group. All recipients of blood were given quinine.

B G P SHAYKOFF, M.D.

OPERATIVE SURGERY AND TECHNIQUE POSTOPERATIVE TREATMENT

Marshall, D. V. Pulsator Treatment of Crush Injuries. *Lancet* Lond., 1944, 247, 562.

Four cases of crush injury which occurred two years ago after an air raid are recorded; the results were unexpectedly good. The Booth respirator was used in their treatment. The author has had no opportunity of trying the method in additional cases.

During the severe raids in the spring of 1941 quite a number of patients having been buried under masonry and extracted after varying periods of time (from four to ten hours) came to hospital showing little in the way of external or internal injuries but soon after their limbs became numb and swollen and about forty-eight hours after admission they suddenly became ill and died the next day or later blood being found in the urine some hours beforehand. One patient's arm was treated for about ten hours in a Booth respirator before she was transferred to a hospital in the country. The patient said her arm felt very much better after the treatments and it recovered quickly. This incident prompted the author to treat all of the crush injuries which came under his care in York in the Booth respirator.

As soon as possible after the diagnosis of crush injury was made the damaged limb or limbs were placed in the respirator and the pulsation mechanism was worked at the slowest rate provided for about half an hour. Four patients received treatment for this period every two or three hours in rotation. The treatment was continued regularly except during sleep until the circulation of the affected parts seemed to be restored as judged by the diminution of pain, return of warmth and color, and loss of tension. All of the patients recovered, and 3 said

that their pain was much reduced by the treatment and that they felt generally better. The patient who was injured least and who was mentally clearest was most emphatic on this point. One woman who was most severely crushed and who complained of so much pain that at first it was thought she had fractured pelvis in addition to her leg injury, did not experience relief and found moving from the bed in and out of the respirator rather trying.

Most of the efforts in treatment have been concerned with preventing renal damage by medication or treatment directed toward relieving the kidneys or preventing the toxin from getting to the kidneys in large amounts after damage has occurred. The treatment is also aimed at preventing changes in the muscle by relieving or improving the circulation at the earliest moment.

It is suggested that the fatal result of the crush injury syndrome may be prevented by prompt restoration of the circulation in the affected part with a mechanical pulsator. JOHN E. KIRKPATRICK, M.D.

Swenson, S. A. Jr., Harkins, H. N., and Grossbeck, H. P.: Pilonidal Sinus. Clinical Experiences with the Rogers Operation in 35 Consecutive Cases. *Am. J. Surg.* 1944, 66, 49.

The authors report their experiences with the Rogers operation in 35 consecutive cases of pilonidal sinus. They state that with this procedure there is complete removal of the diseased tissue, healing takes place in the presence of infection, the rate of recurrence is low and the patient loses little or no time from his work.

Local novocain anesthesia was used in 20 cases; spinocaine in 14 cases and general anesthesia in 1 case. In this series the Bowie cautery was used on hospitalized patients and a modified radio-cautery was used on outpatients. A narrow ellipse of skin was marked out above the sinus tract or cyst. Healing was more rapid in the cases which did not have overhanging edges. The authors state that the use of the cautery knife provides a bloodless field which aids in the recognition of unstained normal tissue.

Diseased tissue is less readily divided by the cautery knife than is normal tissue. The dissection is carried down to but does not divide the diseased tissue in the attempt to remove the tract en bloc. The defect resulting from the removal of the diseased tissue is packed with dry gauze and a small dressing is applied. Outpatients are permitted to go home immediately and they may return to work.

The first change of dressings is carried out on the fifth or the sixth day and a new pack is inserted. This pack is allowed to remain for two days, and on the third day it is removed in a sitz bath. The patient then takes two sitz baths a day applying a dry sterile dressing after each bath. He returns to the clinic twice a week until the terminal stages of healing after which he reports weekly.

Hospital patients are treated similarly. Frequent visits to the clinic are recommended as being more

important during the last few weeks of healing because the whole success of this method of treatment depends upon proper care, preferably by the original operator.

In this series of 35 cases 25 per cent of the patients were females, and 75 per cent were males. The average age was twenty-six years. Seventeen of the patients were from twenty to twenty-nine years. Fifteen patients had known of their lesions for one year or less. 15 had had previous or preliminary treatment. In 24 patients the duration of the drainage was from one week to two months. Twenty-four patients presented only one sinus tract. In 23 patients the inpatient procedure was carried out and in 12 the "out-patient" treatment was given. In the cases of the 3 hospital patients, the average stay was six and one half days. The average number of postoperative visits was 10 and the average healing time in 30 cases was fourteen and one half weeks.

The advantages of this procedure are the low cost, the small amount of tissue removed, and the high percentage of primary cures.

RICHARD J. BERRYETT JR., M.D.

Zintal, H. A., Riegel, C., Peters, R., Rhoads, J. E., and Ravdin, I. S. Intravenous Administration of Dextrose in the Treatment of Patients with Disease of the Biliary Tract. *Arch. Surg.* 1944, 49, 38.

Biopsy specimens of the liver were taken from a group of 58 patients with disease of the biliary tract. Eighteen of these patients received dextrose intravenously before operation while the remaining 40 were controls and received none. The average glycogen level of the liver of the patients who received dextrose intravenously was 6.1 per cent, or 118 per cent greater than the average glycogen level of the control group.

The patients who had moderate hepatic damage, as judged by histological studies and who received dextrose intravenously had an average hepatic glycogen level of 5.7 per cent, or 104 per cent more than the level observed in the control patients. Intravenous administration of dextrose without dietary supplement did not significantly lower the fat content of the liver in the patients observed.

The authors state that the protection of the liver against damage resolves itself into the positive action of protein, the indirect action of carbohydrate, and the negative action of fat. The results of administration of a diet high in carbohydrate and protein, low in fat, and high in calories for five days or more before operation while excellent from the standpoint of reducing the fat content of the liver were not impressive from the standpoint of the degree of elevation of the glycogen level. The average increase of liver glycogen after such a diet in patients with severe hepatic damage was 10 per cent. On the other hand there was no evidence in the patients who received dextrose intravenously that the fat content was significantly lowered.

In the light of these findings, the optimum preparation of patients with hepatic damage for surgery operation would probably be obtained with the administration of a diet high in protein and carbohydrate and low in fat for a period of from five to fourteen days, supplemented by intravenously administered dextrose for a period immediately prior to operation.

Liver glycogen is so labile that if one desires to maintain it at a high level during an operation, intravenous administration of dextrose is fully justified especially during the period of fasting immediately before operation. As much as 45 per cent of the liver glycogen may be lost during the course of a long operation as reported by Ariel Pack, and Rhoads.

HARRIET F. THURSTON, M.D.

Brown, J. B., and Cannon, B.: The Repair of Surface Defects of the Foot. *Ann. Surg.* 1944, 30, 412.

The skin and subcutaneous tissues of the sole of the foot and of the palm of the hand constitute a specialized organ. Skin and subcutaneous tissue transplanted to the sole of the foot from other areas of the body do not constitute a normal sole and there may be difficulty in maintaining them in a satisfactory condition in their new environment and function. Keratosis, warts, cracks and chronic ulcers may appear and cause disability. If nerves are present in the area of the sole, even in free grafts and flap sensation will return.

Small lesions of the foot may produce disability and especially in military service may cause complete loss of a soldier because one of the most important functions of a soldier is lost if he cannot walk.

The preoperative care includes rest, baths, soap and water sulfonamides or penicillin, fine mesh gauze next to open wounds, pressure dressings, and elastic bandaging of the foot and leg. Every effort is made to get these wounds as clean as possible, guided by bacteriological studies. No repair or operation may be even contemplated until all abscesses, dead tendons, fascia, and bone are out of the wound. There must also be good healing power which it support transplanted tissue. Physical therapy is used in all cases.

When a flap is lost, the donor site may be worse than the original lesion. Radical excision must be carried out in widespread scars so that a new blood supply may be developed to support the transplanted tissues. Burns and superficial lesions respond well to free grafts although gunshot and shell-fragment wounds or other deep injuries may require a flap repair. Flaps will not do well where grafts will do well. A distant flap does not bring additional blood supply but just helps the local minute blood supply temporarily. Local flaps bring in their own blood supply and improve the local circulation. Local flaps may deprive another area of a satisfactory covering and may cause loss of important local sensory nerves. Local flaps which uncover important weight bearing points, the heel cord, or the malleoli, should not be used.

The methods of repair include

1. Excision of the scars and immediate resuture. This may be carried out only occasionally because of lack of extra tissue in the foot. Large losses practically always need some type of replacement even though it proves a poor substitute.

2. Free skin grafts may be used if a satisfactory thickness of subcutaneous tissue remains to give support and blood supply. Open wounds on the sole of the foot are subject to severe disabling infections and should be closed as soon as possible. Free grafts may be used to get the wound closed as soon as possible, and later on a flap may be used for permanent closure.

3. Direct local flaps may give excellent repairs of small lesions if important sensation is not interrupted and both the local blood supply and the blood supply of the flap is adequate.

4. Delayed local flaps are the safest form to use locally; at least two stages of operation should be used. Detachment of flaps may usually be carried out in from sixteen to twenty days. In large flaps, partial detachment in 2 or 3 stages may be carried out with more safety.

5. Direct cross-leg flaps may be used if a suitable position can be decided upon.

6. Delayed cross-leg flaps either flat or tubed are safest.

7. Same-leg delayed flaps may be used occasionally they should be tubed rather than flat.

8. Distant turnover jump or caterpillar flaps from the abdomen or flank are a rare necessity.

9. Distant wrist borne flaps are used occasionally. Tubed flaps need a special type of application. Large long tubes should be attached in a normal site close to the defects.

One of the most difficult problems in postoperative care is to keep the patient off the new repair for a sufficient length of time. Local trauma and extremes of temperature should be avoided.

A wide knowledge of the faults of flaps and grafts must be acquired so that these difficulties may be guarded against. Ordinary skin will not change into normal foot tissue and continued protection clean lines careful observation and pads are necessary. Prevention is better than cure. Some surgeons believe that only sole tissue should be used on the sole. The end results in skin repair of the foot vary from poor to practically normal. Prolonged disability has been relieved by single procedures.

RICHARD J. BIGNETT JR., M.D.

Young, F: Skin-Graft Fixation by Plasma-Thrombin Adhesion. *Ann. Surg.*, 1944, 120: 450.

The author notes that the survival of a free skin graft depends upon the rapid establishment of an adequate circulation. During the first twelve to twenty four hours after transplantation it is generally believed that there is an osmotic flow of plasma into the graft.

The early vascularization of a skin graft may be delayed or prevented by numerous factors. The graft may be too thick or of too great area for the

vascularity of the bed in question. A full thickness skin graft will rarely take on a granulating surface. Full-thickness grafts when applied to fresh surgical wounds have a higher percentage of take when the graft is from a thin skin area such as the groin inner surface of the upper arm, or eyelid. It is also well known that full thickness grafts have a higher percentage of take than those of large square area since in the smaller graft the peripheral circulation established is relatively of more importance. In general the thinner and smaller the graft the higher percentage of success.

The character of the bed is important for the survival of the free skin graft. A high percentage of take cannot be expected on an avascular fibrotic bed. The percentage of take is usually lower on a soft yielding irregular surface than on a smooth firm bed.

There are numerous untoward effects which can prevent complete continuous contact. The graft may slip off of the recipient area or it may be lifted off the bed by bleeding. Infection may cause the formation of purulent exudate under the graft and on irregular surfaces the graft may be stretched across depressions and the bed may move unless adequately splinted.

In the past a high percentage of takes has been obtained by careful attention to many details one of which was the use of compression dressings to keep the graft firmly in contact with all irregularities of the bed. Joints were splinted and unlay forms used on parts where splinting was not possible.

Fixation of split thickness grafts on either fresh surgical wounds or granulating beds can be accomplished by the precipitation of fibrin between the graft and the bed by adding thrombin to plasma. The rate of fibrin formation can be adjusted to any speed desired by increasing or decreasing the concentration of the thrombin solution.

The author states that 22 separate free split thickness skin grafts were applied with the use of fibrin and without pressure dressings or suture. On extremities where the part could be suspended no dressing whatever was used. On other parts merely a loose dry gauze for protection was applied. The amount of skin transferred at one operation has varied from 4 square inches to 200 square inches. The majority of cases were wounds of considerable dimension usually exceeding 30 square inches. The exact procedure followed in making the graft is given in detail as well as the preparation of the fibrin.

Because the percentage of take normally expected on fresh wounds is higher than on granulation tissue, the author divides these cases into two groups. Of 12 patients with a primary graft 8 had free grafts placed on fresh surgical beds. There was no loss in this group. In each case the graft take was complete. The 4 remaining patients in whom the bed was fresh had traumatic contaminated wounds. In these the percentage of take was 48. The figure was lowered by total loss of the graft in 1 instance. In the 10 granulating wounds a 59 per cent average take was

estimated. In 2 instances the graft was lost completely. In all of the instances it was evident that the loss of graft was due to the accumulation of fluid under it. Large bulbous areas form most of which, when opened, are found to contain purulent fluid.

On fresh surgical beds the percentage of take of free skin grafts is ordinarily high, and fixation by plasma thrombin adhesion seems to afford an easy method of obtaining the usual high percentage of take. However it is the impression of the author that in infected wounds the loss of grafts is considerably greater when they are applied by this method than when compression dressings are used. This applies to contaminated fresh wounds as well as to granulating beds. Infection is sealed under the graft, drainage is poor and the result is a purulent collection under the graft which prevents vascularization. The greatest loss is at points of movement. This could be prevented by splinting. Small-size thin grafts take better than large thick sheets. It is probable that the mere application of the dressing would produce as high a percentage of take alone.

In conclusion the author states that he believes the method is useful (1) in application of grafts on fresh surgical beds, (2) in holding grafts in position while compression dressings are applied and (3) in applying small grafts such as pinch grafts for which compression dressings are ordinarily not used.

HENRY F. THURSTON, M.D.

Webster J. P.: Refrigerated Skin Grafts. *J. Surg.* 1944, 20: 431.

Refrigerated grafts are seldom used in surgery today although the technique is simple and its application has widespread uses. It is of special value in grafting young, debilitated, or extensively burned patients. The source of the grafts may be cadavers, amputated limbs as homografts or autografts, or the usual donor areas on trunk or limb of the patient himself or of others. Only autogenous skin grafts may be expected to survive permanently.

The procedure has been employed 36 times on 23 patients at the author's clinic during the past twelve years. All of the grafts lived if the recipient areas were suitable and if the grafts were autogenous and were not refrigerated for more than three weeks. In the author's experience those refrigerated over this period failed to survive. No homograft persisted permanently although those refrigerated within the three-week period survived longer than those preserved beyond this time. Lyophilized skin was grafted in 1 case with partial but definite success after seventeen days of refrigeration. This procedure gives promise of being improved and of value. With a modified technique it may be possible to graft lyophilized skin with even greater success and beyond the three-week period of refrigeration.

The refrigeration of skin should be more widely used (a) to store excess remnants of grafts for possible future use, (b) to delay grafting until suitable conditions of the recipient area prevail and (c) to

divide long hazardous operations into two or more less taxing stages. By this procedure the plan of operations may be facilitated and lives may be saved.

LOUIS T. BYARS, M.D.

Crooke A. C., Morria, C. J. O. R. and Bowler R. G.: Plasma Volume in Traumatic Shock. *Brit. M. J.*, 1944, 521.

The plasma volume (by the Evans blue dye method) hemoglobin and hematocrit were measured in a series of patients suffering from traumatic shock. Corrections and technique modifications were made to overcome anomalous dye concentrations in the plasma due to turbidity, hemolysis, and the effect of morphine and hyoscine. A reduction in plasma volume was characteristic during shock and was proportional to the severity of shock. The test was most significant when determined early.

In the severe cases reduction of the plasma volume averaged about 2 per cent of the body weight. In this series the author did not confirm Moon's correlation of shock with hemoconcentration as manifested by increased values for the hemoglobin and hematocrit cell volume. Rather a reduction in the hemoglobin concentration was noted. This did not parallel the fall in plasma volume, but continued to fall as water was withdrawn from the tissues into the circulation, and became most pronounced after the plasma volume returned to normal. The conception of hemoconcentration in shock, according to the author, originates from the viscid, cyanosed appearance of the blood when examined with the Tiselius electrophoretic apparatus is not found to be correct.

B. G. P. SCHARROFF, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Kendry W. E.: The Prognosis in Acute Hematogenous Osteomyelitis with and without Chemotherapy. *Surgery* 1944, 16: 477.

The mortality in acute hematogenous osteomyelitis before chemotherapy was 23 per cent on the average, 46 per cent in the toxic cases and about 3 per cent in the nontoxic cases. After sulfonamide therapy was introduced it was 3.5 per cent.

Previous to the use of the drug, early bone decompression was almost prohibited by the severe mortality. Yet early bone decompression yielded the best results from the standpoints of the later integrity of the bone and function of the limb.

Incision down to the bone, aspiration, or withholding operation either before or after the administration of sulfonamides has not given as satisfactory results as early bone decompression. The new drugs, by controlling the initial septicemia and that which may follow operative intervention, have not allowed safe, early procedures.

The sulfonamide drugs have not proved of value so far as the local pathological process is concerned. One must still depend upon operation for the best results.

This study has been based on the reported experiences of surgeons with 3 176 cases of acute hematogenous osteomyelitis

BENJAMIN GOLDMAN, M.D.

Eliass, D. G. Fuller A. T. and Walker J.: New Drugs Active in the Chemotherapy of Experimental Gas Gangrene. *Lancet* Lond. 1944, 247 553.

Two new drugs p-methylsulfonfylbenzamide hydrochloride (V187) and p-methylsulfonfylbenzylamine hydrochloride (V335) have been synthesized and found to have a potent local chemotherapeutic action in experimental gas-gangrene infections in guinea pigs. Their action is not inhibited by p-aminobenzoic acid.

An extended study of V187 has demonstrated its effectiveness against clostridium welchii, oedematis, and septicum infections. It is well tolerated when given intramuscularly in therapeutic doses. In vitro and in the mouse V187 is as effective against sulfanilamide-resistant streptococci as it is against sulfanilamide-sensitive strains.

In guinea pigs V187 is rapidly absorbed and excreted after intramuscular and intraperitoneal administration. Given orally it is but poorly absorbed.

HAROLD C. OCHSNER, M.D.

Tate, B. C., and Klorofaj I. Sulfonamide Dermatitis; Further Observations. With Special Reference to Treatment and Prevention. *Lancet*, Lond. 1944, 247 553.

In a previous article the author described epidermal sensitization caused by the local application of sulfonamides to the skin. A procedure for desensitization was outlined but the attendant reactions were often extremely severe. The method has now been modified so that complete desensitization is achieved with a minimum of discomfort. A means of preventing this type of sensitization has also been devised. Nearly all of the authors' patients were sensitized originally to sulfanilamide possibly this drug produces a wider range of sensitization than sulfathiazole.

The original procedure was to give relatively large doses by mouth daily and continue giving them in spite of the resulting eczema until the reaction subsided. It became apparent, however, that the quantity of drug required varied with the degree and extent of sensitization and it was also found that there is a threshold dose for each patient below which no reaction occurs and amounts slightly in excess of this produce only mild symptoms. Therefore, it seemed probable that a dose between the minimum threshold dose and that producing a maximum reaction would desensitize with little discomfort to the patient provided treatment were sufficiently prolonged. Experience has confirmed this supposition and the method has been successfully employed in 30 cases.

The correlation between the degree of sensitization and the quantity of drug required was more ap-

parent with the intermediate doses than when large doses were employed. A point of equal importance is the duration of treatment, e.g. 3.0 gm. spread evenly over two or three weeks produce far more complete desensitization than a larger dose given in one day.

Treatment should not be started until any eruption from previous contact with, or administration of the drug has disappeared otherwise symptoms may be unnecessarily severe. Exposure to direct sunshine may greatly aggravate the reaction and must be avoided. A check on the leucocyte count is of course, advisable.

If desensitization results from neutralization of the antibody it should be possible to prevent sensitization by using up the antibody as fast as it is formed. It should indeed be safe to apply the drug locally provided it is given simultaneously by mouth in adequate doses this hypothesis can be proved only by treating sensitized patients in this manner.

The phenomena of this type of sensitization are most easily explained although the explanation is not necessarily correct, by the assumption that some new substance is formed by the epidermis to which it remains fixed. In accordance with common usage this hypothetical substance has been called antibody.

Desensitization presumably results from neutralization of the antibody with allergen. Strongly supporting this hypothesis is the correlation between the degree of sensitization and the quantity of allergen required for desensitization and, more conclusive still the disappearance of sulfanilamide from the blood after its administration to a sensitized patient. However re-sensitization and reappearance of the drug in the blood after too brief treatment show that the reaction between allergen and antibody (simple neutralization as between acids and bases) is a reversible one which is governed by the law of mass action the products of which are only slowly eliminated.

The time required for excretion of the allergen-antibody compound seems to be about fourteen days because, for complete desensitization this is the period over which, it has been observed, the drug must be continued after a large increase of dose has failed to cause symptoms—i.e. presumably after the whole of the antibody has been neutralized. The rate of this excretion may vary in different subjects hence the authors have insisted on a final test of one large dose.

The constitutional symptoms which accompanied desensitization in some cases (rigors raised temperatures fainting blood changes) are essentially manifestations of anaphylactic shock. Their occurrence does not mean however that other organs besides the epidermis were sensitized.

Although no evidence of systemic sensitization has so far been encountered there is no guarantee that it will not develop and the question arises whether this risk should be taken. For most in factive dermatoses local sulfonamide therapy is not superior to other methods of treatment in the

authors' experience but there are instances in which it seems to be of great value and since the main objection to it has been removed by preventive oral therapy, its employment in carefully selected cases is considered justifiable.

The statements in this article are confined to epidermal sensitization to the sulfonamides but the method of desensitization has proved equally successful in acriflavine and boric-acid dermatitis. The authors believe that the principles mentioned are applicable to the wider field of allergy in general.

JORDAN E. KIRKPATRICK, M.D.

Vlter C. F., and Blankenhorn M. A.: The Toxic Reactions of the Newer Sulfonamides. *J. Am. M. Ass.* 944 6 69

In the past four years 1,036 patients in the medical wards at the Cincinnati General Hospital have been treated with sulfathiazole, sulfadiazine, sulfapyridine, sulfaguanidine and succinylsulfathiazole. Sulfapyridine is now considered obsolete and is no longer used in this service. Sulfanilamide is rarely employed and only a preliminary report can be given on sulfamerazine since its use has been recent. This particular study was undertaken to determine the relative incidence of untoward reactions to the various drugs and the relation of the mild and readily recognizable symptoms to severely toxic or lethal reactions. Difficulties were encountered in this evaluation because many patients admitted to this service are critically ill as the result of acute infection or they are in a moribund state of chronic disease and thus the differentiation of symptoms due to drug from those due to disease is difficult. Also the drug is usually discontinued at the first sign suggestive of sulfonamide toxicity. Consequently the course from early and mild to late and severe symptoms can rarely be followed.

Unfortunately there is no absolute method, short of discontinuing the sulfonamide, of differentiating such fever from that produced by the infection for which the drug is given. Frequently, however, there are clinical signs of resolution of the infection, or one is aided by the appearance of skin manifestations.

Skin lesions usually appear between the second and tenth days. Sulfathiazole usually produces a tender erythema nodosum, most frequently found on the extensor surfaces of the extremities and on the face. Sulfathiazole may also produce a morbilliform erythematous rash, either localized or widespread. The skin lesions may become pustular with continued administration of the drug.

Conjunctivitis frequently associated with erythema nodosum, occurred only in patients treated with sulfathiazole. It occurred between the fifth and fourteenth days and was bilateral in all but 1 case. The erythema and moderate edema of the bulbar conjunctiva may be accompanied by burning of the eyes and photophobia.

Nausea and vomiting, distressing symptoms that contributed to the discarding of sulfapyridine, occur infrequently with sulfathiazole and rarely with sulfa-

diazine. They usually appear after the first dose of the drug, in contrast to similar symptoms which may appear later as a result of uremia due to sulfonamide nephrosis or tubular obstruction. It is usually possible to change immediately to another sulfonamide with prompt relief of the emesis.

Polyneuritis, which is usually asymmetrical, has a remarkably high incidence. Its onset with pain, burning numbness or tingling has occurred as early as the seventh day of treatment and perhaps as late as six months after a course of sulfonamide.

Delirium is difficult to attribute to sulfonamides, since it occurs so frequently in febrile disorders. As a rule, it occurs in association with other toxic manifestations of the drugs, particularly renal complications.

Polyarthritides and arthralgia appeared in a small number of the cases between the second and tenth days.

Alterations in the blood and bone marrow are noted 11 times with sulfathiazole, once with sulfapyridine and not at all with sulfadiazine. These reactions may occur at any time in the course of therapy. Leucopenia gives no clinical sign. Thrombocytopenia is, of course, usually associated with hemorrhagic phenomena, hemolytic anemia, jaundice and agranulocytosis with dirty ulceration of the mouth and pharynx. None of the toxic symptoms are of particularly deadly portent. Most of them disappear within one or two days after discontinuance of the sulfonamide, except that neuritis may not. Leucopenia may disappear even while treatment with the sulfonamide continues. When the onset of peripheral neuritis occurs during treatment, the necessity of treatment must be weighed against the possibility of a persistent neuritis after recovery. Thiamine has not cured or prevented the form of neuritis.

The most troublesome toxic symptoms center about the kidney and the urinary tract. These have been the most dangerous to the patient and most difficult to diagnose in the early stages. They appear in two separate forms but may overlap. The one is a mechanical obstruction of the renal pelvis or ureter by crystals, the other is injury of the secreting portion of the kidney.

Sulfonamide nephrosis, characterized by drug retention and a rising blood-urea nitrogen may or may not be accompanied by oliguria and anuria and by albuminuria. It has occurred in patients receiving sodium bicarbonate. It may occur in conjunction with a systemic picture of encephalopathy, myocarditis, hepatitis, anemia, leucocytosis, and fever, and is readily confused with Weil's disease when the history of sulfonamide ingestion is lacking. It appeared in 10 of the cases collected and the smallest dose of drug (sulfathiazol) was 6 gm. The anuria noted regularly between the first and fifth days that the first manifestation was a rising blood-urea nitrogen level.

The treatment of renal complications must suit the individual case. Because of the frequency of

which renal complications occur daily determinations of the fluid intake and urinary output and frequent examinations of the urine for erythrocytes and of the blood for the drug level and nonprotein nitrogen should be routine procedures. For hematuria the urine should be alkalinized promptly by the administration of sodium bicarbonate and fluids should be administered to bring the urinary output to at least 1000 cc. per day. If oliguria or retention of drug or nonprotein nitrogen develops the fluid intake should be increased, but if improvement does not result the drug should be discontinued. Ureteral catheterization is indicated if anuria is preceded by hematuria and renal colic.

The value of routine alkali treatment concomitant with the sulfonamides is still open to question. Although it is true that sulfonamides are more soluble in alkaline solutions and consequently might have less opportunity of depositing themselves in the genitourinary tract, the increased rate of excretion tends to reduce the blood level of the sulfonamide to below effective range.

With advanced age and renal disease, sulfonamides should be prescribed cautiously and the treatment followed carefully. With the onset of persistent hematuria, decreased urine output, signs of azotemia and unusually high levels of sulfonamide in the blood, or of any one of these manifestations treatment should certainly be discontinued.

It is obvious that the early signs of severe reactions are so occult as to be revealed usually only by laboratory studies. There is nothing unfortunately that bedside appraisal of the patient will yield in the early diagnosis of the fatal sulfonamide reaction.

BENJAMIN GOLDMAN, M.D.

Lyons, C. The Re-Evaluation of Sulfu Drugs. *M.D. Surgeon* 1944, 95 301

The toxic reactions from sulfonamides have complicated but have not seriously limited treatment. It is unlikely that new sulfonamides will be more bacteriostatic than the presently available drugs but less toxic compounds may be anticipated.

Prophylactic therapy has prevented invasive systemic infection and minimized the spread of local infections. This success suggests the oral or parenteral route as a method of choice.

Good clinical evidence for or against the continued local use of sulfonamide preparations in wounds is not available. Rapid absorption after intraperitoneal application makes it difficult to evaluate the abdominal cases in terms of local therapy. Considerable doubt prevails about the value of sulfonamides in the prophylaxis of gas gangrene. A distinct trend away from local sulfonamide therapy exists but individual preference and opinion continue to guide such practice.

General hospitals in this country are receiving casualties with chronic infections associated with retained sequestra or foreign bodies. These infections are sulfa resistant and many of the patients are sulfa-sensitive. The associated debilitated state

contraindicates intensive sulfa therapy. Such cases are more often surgical failures than sulfonamide failures but they represent a group of infections requiring some form of antibacterial therapy other than that with sulfonamides. The need for continued study of surgical infections is evident.

JOSEPH GASTER, M.D.

Bigger, J. W.: The Treatment of Staphylococcal Infections with Penicillin by Intermittent Sterilization. *Lancet* Lond. 1944, 247 497

Experimental evidence is presented to show that penicillin, although bactericidal failed to sterilize completely broth cultures of the staphylococcus pyogenes. This can be accounted for on the basis of a constant proportion of cocci which are insensitive to penicillin. The latter are characterized as persisters because of a temporary resistance to penicillin while they are in a dormant nondividing phase. However dormancy lasts for a few days and with resumption of bacterial division the organisms again become susceptible to the action of penicillin and are destroyed by it.

Clinical evidence also suggests that the same process takes place in vivo. In cases of staphylococcal osteomyelitis treated with penicillin there may be a return of activity of the disease after treatment is stopped. This may be accounted for on the basis of the survival of persisters in the infective focus which begin to multiply after the bacteriostatic action of penicillin is stopped. Polymorphonuclear leucocytes can destroy such persister cocci only slowly.

A fractional or intermittent method of sterilization is recommended to destroy all the bacteria over a period of nineteen days. This method provides for the maintenance of $\frac{1}{4}$ to 1 unit of penicillin per cubic centimeter of the patient's serum and requires 400,000 units of penicillin per twenty four hour treatment period. The plan provides for a first treatment period of four days, followed by an intermission of one day and four other treatment periods each of two days with intermission periods of one day.

In order to obtain a prompt high concentration of penicillin an intramuscular injection of 30,000 units should be given initially together with a daily continuous intramuscular drip of 100 cc. of saline solution containing 400,000 units. This method of therapy does not preclude the surgical evacuation of collections of pus which serve as reservoirs of persisters. The author also suggests that the findings described are applicable to penicillin-sensitive non hemolytic streptococci. B. G. P. SHATTUCK, M.D.

Coleman, R. and Sako, W.: The Treatment of Multiple Furunculosis with Penicillin. *J. Am. M. Ass.* 1944, 126 427

The incidence of furunculosis superimposed upon millaria is much increased during the warm summer weather. In the South this condition constitutes a common problem which often proves to be very

refractory to treatment. A remarkably rapid response of multiple furunculosis to intramuscular penicillin therapy has been observed in 6 young children. Histories of the 6 cases are reported.

SAMUEL KAHN, M.D.

McKissock, W. Logue, V., and Bartholomew, I.: The Need for Asapels in Local Penicillin Therapy. *Brit. M. J.* 1944, 55

A study of the Preliminary Report to the War Office and Medical Research Council on Penicillin by Florey and Cairns in 1943 reveals that Gram-negative organisms have been found in the discharge from penicillin-treated wounds. In some cases such organisms as the bacterium coli, proteus vulgaris and pseudomonas pyocyanus have been grown from the aspirate from wounds receiving local injections of penicillin solution, and in others they have been cultured from pus issuing from similar wounds before healing was complete. Often enough the presence of such organisms either in aspirated fluid or in purulent discharge, appeared to cause no serious complication or to delay healing unduly. The bacteriological results usually showed that after two days of treatment of the brain cavity with penicillin Gram positive cocci were no longer found in the fluid sucked or discharged from the wound but organisms of the coliform group were almost invariably present. In wounds which remained completely closed this state of affairs persisted until healing was complete. Such Gram negative organisms are present in the wound initially but are overgrown by staphylococci and streptococci in first cultures. Their presence is but another example of added hospital or cross-infection of wounds.

The opportunity for cross-infection of a wound undergoing treatment with penicillin solution is particularly good. A rubber tube runs from the outside air to the depths of the wound and through this channel injections of the penicillin solution are made usually twice daily for a period of from three to five days.

Three main points may be responsible for the very low rate of hospital or cross-infection of wounds: (1) the care taken in closing scalp wounds to obtain very early healing; (2) the insistence upon very careful ward and dressing technique; and (3) an aseptic cap used to close the penicillin tube.

The incidence of potential cross-infection was 3 cases among 30 in the unit's original surroundings, but no clinical cross-infection occurred. In a second series under less perfect conditions the potential rate rose to 7 cases among 30 (35 per cent) and 1 superficial case of clinical hospital infection resulted (5 per cent).

HARRY W. FINE, M.D.

Griep, L. H.: Allergy to Penicillin. *J. Am. M. Ass.* 1944, 126 439.

A case of penicillin allergy manifested by generalized severe urticaria and studied from the point of view of the possible immunology involved, is reported.

This allergy in all probability is not unlike that of serum allergy. As is the case in other instances of sensitization to biological products, such as insulin, the posterior lobe of the pituitary gland and liver extract the reaction occurred after the resumption of treatment following a period without treatment.

There seems to be evidence of the presence of some immune substances in the serum of the patient, such as reagins and precipitins. This is proved by the positive direct skin test, by the positive passive transfer and the positive precipitin test. What role if any these antibodies might have in mediating the reaction is not exactly clear.

The allergy to penicillin is probably unrelated to sensitivity to penicillium spores.

SAMUEL KAHN, M.D.

Bloomfield, A. L., Kirby, W. M., and Armstrong, C. D.: A Study of "Penicillin Failures." *J. Am. M. Ass.* 1944, 126 685.

From an intensive study of more than 100 patients treated with penicillin a good deal has been learned about what might be called "penicillin failures" and it is with this phase of the subject that the present article is concerned. Penicillin failures may be discussed under the following headings:

- 1 Causes of death in penicillin treated patients
- 2 Failures due to inadequate amounts of penicillin.
- 3 Failures due to inadequate surgical drainage in penicillin-treated cases
- 4 Failures due to overwhelming infection even when penicillin dosage was presumably adequate.
- 5 Failure to prevent or cure renal lesions in penicillin treated cases of streptococcal infection.
- 6 Conditions in which penicillin either fails or is likely to be inadequate.

1 Causes of death in penicillin-treated cases. Aside from patients not seriously ill, 87 instances of severe infection, including endocarditis, meningitis, and acute osteomyelitis have been treated. Of this series 7 or 8 per cent terminated fatally. It appears that only 2 deaths or 2.3 per cent, of the whole series could be ascribed to the actual failure of penicillin treatment. Ten years ago one would have had a mortality of at least 50 per cent.

2 Failures due to insufficient penicillin therapy. Excellent results have been reported with relatively small quantities of the material but this does not rule out the need of larger doses in some cases. At any rate the unsatisfactory results in the reported series seemed to be ascribable to too small amounts of penicillin or to treatment of too brief duration.

It seems clear that with any serious infection it may be well to continue treatment for several days after the process has been controlled as a possible insurance against recurrence. This applies especially to staphylococcal and streptococcal infections. In subacute bacterial endocarditis due to the streptococcus viridans the good results which are obtained in a consecutive series of 9 cases seemed to be due to the continuation of uninterrupted treat-

ment over a period of from six to eight weeks. Recurrences of acute hemolytic streptococcal throat infections common with brief treatment can be prevented by giving penicillin over a period of from five to ten days.

An analysis of 8 cases of acute osteomyelitis of the long bones in which no operation was done indicates that very intensive and prolonged therapy is necessary if serious changes are to be prevented. Even then, the roentgenograms from the second week on usually show some absorption of the cortex with periosteal reaction, possibly due to injury which began before penicillin therapy was started. Some staphylococci must be sealed in and be difficult to reach in areas made relatively avascular by thrombosis and necrosis. Prolonged uninterrupted treatment is clearly indicated in acute osteomyelitis.

3. Failures associated with penicillin therapy when adequate surgical drainage of infections was not carried out. In spite of the great efficacy of penicillin in controlling certain types of infection the principle that evacuation of closed collections of pus is necessary for rapid cure still holds good in most cases. Simple aspiration of pneumococcal empyema and of gonococcal joints with the injection of penicillin, has been adequate in many cases but in other infections especially those due to staphylococci and nonhemolytic streptococci progress may be arrested until surgical drainage has been instituted.

4. Failures due to overwhelming infection. One patient provided the only example of failure of penicillin due simply to an overwhelming infection with an organism sensitive *in vitro*. She received large doses of penicillin by continuous intravenous drip sufficient to raise the blood content to well over the standard bacteriostatic level of 0.15 unit per cubic centimeter. In spite of this the blood stream was not cleared and after twenty hours culture still yielded 130 colonies of staphylococcus aureus per cubic centimeter. The importance of using penicillinase is also brought out, as there was enough penicillin in the blood to inhibit growth in a blood culture made without penicillinase.

5. Failure to prevent or cure the development of glomerular nephritis in certain patients with streptococcal infections treated with penicillin. The association of glomerulonephritis with certain types of streptococcal infection is clearly established. When penicillin became available it seemed of particular importance to find out if this agent which estimates so many streptococcal infections with great speed would prevent the occurrence of nephritis. Of no less interest was the question of whether nephritis already established would clear up after the elimination of concomitant streptococcal infection by penicillin, as for example in bacterial endocarditis.

There is no evidence that the course of nephritis is influenced, but every reason to believe that when an irreversible lesion has been set up it will progress in the usual relentless fashion of chronic glomerulo-

nephritis. Similar observations by one of the authors (C.D.A.) in cases of bacterial endocarditis due to the streptococcus viridans have shown that the renal lesion may persist after the infection has been eliminated. All this is in harmony with the evidence accumulated by Addis to the effect that glomerular nephritis once under way tends to propagate itself.

6. Conditions in which penicillin either fails or is likely to be inadequate.

Pneumococcal meningitis.—Although pneumococci are often highly sensitive to penicillin the results of treatment of pneumococcal meningitis have been unsatisfactory in many ways. These poor results are doubtless attributable in some degree to the nature of this infection with its well known tendency toward adhesive arachnoiditis, encephalitis and thick gelatinous exudate which impedes the local application of any therapeutic agent. Since sulfonamides are quite effective in pneumococcal meningitis it may turn out that sulfonamides together with penicillin may be the best treatment.

Chronic (staphylococcal) osteomyelitis.—In contrast to the results in acute staphylococcal osteomyelitis the results in most of the chronic cases have been unsatisfactory. If the lesion is in a long bone and can be laid wide open by surgical means, local penicillin irrigations seem to aid in rapid healing. In cases with sinuses leading into the pelvic bones or into the spine (inaccessible to surgery) neither local irrigations nor heavy intramuscular injections have had any definite effect.

7. Conditions in which penicillin was entirely ineffective

Tuberculous paravertebral abscess (no effect)

Lymphoid leucemia (no effect)

Aleukemic myeloid leucemia (no effect)

Infectious mononucleosis (no effect) (This condition developed in a patient with acute osteomyelitis while under active penicillin treatment.)

Mycosis fungoides (no effect)

Chronic (rheumatoid) arthritis (no effect)

Filariasis (no effect) (The blood count of the microfilariae remained unchanged during the penicillin administration.)

8. Relation of penicillin failure to the sensitivity of strains *in vitro*. Even within categories of bacteria such as streptococci and staphylococci and others which are in general sensitive to penicillin there may be strains which are resistant *in vitro*. It is evident that failure of therapy in an individual case may be due to strain resistance and the need of *in vitro* tests in routine work is emphasized.

BENJAMIN GOLDSMAN, M.D.

ANESTHESIA

Arrowood, J. G., and Foldes, F. F.: Subarachnoid Analgesia Maintained by the Continuous Drop Method. *Arch. Surg.* 1944 49 241.

The authors describe a technique for the continuous drop method for maintaining subarachnoid

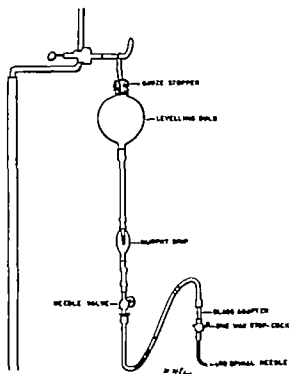


Fig. Diagram of apparatus

analgesia. The equipment consists of a 250 cc leveling flask and tube set with a Murphy dropper

a regulating valve and a glass adapter. The initial dose of anesthesia is given in the same manner as would be used with the fractional method of administration.

The apparatus is then hooked up to the malleable spinal needle. Analgesia is maintained by the drop method. The leveling flask containing 0.5 per cent procaine hydrochloride solution is suspended from 60 to 80 cm. above the level of the spinal needle. About twenty minutes after the initial dose approximately 40 drops of 0.5 procaine solution are permitted to run in. The valve is then carefully regulated so as to deliver the desired number of drops which may vary from 4 drops per minute on up.

Twenty-seven consecutive cases are summarized in table form with details as to the dosage given, the adjuvant anesthesia, and the duration of the operation.

It is believed that this more sensitive method of giving continuous spinal anesthesia will maintain the necessary level of analgesia from moment to moment and will keep the concentration of the drug in the spinal fluid at a minimum at all times. It also provides a perfectly aseptic technique for once connected the system can be kept completely closed at all times.

The safety of the technique depends on its meticulous application and upon expert observation and management of the patient. It is advised therefore that it be used only by the experienced spinal anesthetist who can give it his undivided attention.

MARY KARP M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Wyatt, G. M., and Spurling, R. G. Pantopaque. *Surgery* 1944, 16 561

Pantopaque is the contrast medium of choice for myelography. It is preferable to lipiodol in that it is more readily absorbed and does not remain in the subarachnoid space as a persistent foreign substance. Also, it is nontoxic more fluid than viscous (therefore, it fills out the smaller dural nerve sheaths) more easily removed and it is no more irritating than lipiodol. The sharp roentgenographic contrast which it affords renders it superior to the gases.

The authors were impressed with the rapid absorption of pantopaque which is its chief advantage. Six patients from whom pantopaque was incompletely removed were studied. The entire spine and skull were observed roentgenologically at time intervals varying from one to fifteen months. Absorption was more rapid during the first few months and was retarded over the remaining period eventually absorption was almost complete.

It is believed that the variability in the rate of absorption may be due to the nature of the contrast medium, which is a mixture of isomers. Another factor in favor of rapid absorption is the emulsifying action of body motion on larger collections (0.5 cc) of pantopaque. The medium produces a tissue reaction similar to that of lipiodol when observed after a few months the material was fixed in position. However none of the patients complained of symptoms that could be referred to the residual pantopaque.

MAURICE D. SACHS, M.D.

Hodson, C. J.: Four Primary Roentgenological Lesions Found In Traumatic Chest Cases. A Preliminary Report. *Brit J Radiol* 1944 7 296

Two hundred and fifty thoracic casualties received from within one to twenty-one days after wounding were examined in a thoracic unit in the Mediterranean theater of war.

In 12 cases radiopaque linear shadows were found traversing the lung along the path of the missile. In the early stages, whatever the shape of the lesions they present hazy and ill-defined margins and are often so faint as to be barely visible on the film. In time there is a characteristic change in appearance and at the end of two or three weeks these lesions show plainly as clear-cut linear oval, or rounded shadows from 0.5 to 1.5 cm. in length leading across the lung field to a foreign body or a secondarily damaged rib at the other end. Coincident with this greater clarity of definition is an increase in the density of the shadows. The course is typical over a period of weeks. The lesions slowly become narrower and more opaque until they are lost to sight. When viewed at right angles these tracks show as

definite bands along the course of the missile but when seen end-on or obliquely they become fore-shortened and appear as small oval or rounded shadows suggestive of hematomas or abscesses of the lung. These lesions are similar in nature to missile tracks in other tissue. Postmortem examination in 1 such case showed the lung tissue to be torn along the path of the missile with hemorrhage into the space so formed. Around this central core of blood was a more widely spread area of solid lung due to ecchymosis and edema of the parenchyma which merged gradually into normal tissue. Presumably as the lesion heals the ecchymosis and edema are absorbed and this more solid central core is left to organize which results in a tough fibrous band firmly attached to surrounding structures. One practical point of value of these tracks is that (in 3 cases) they have led to the discovery of foreign bodies otherwise invisible behind the heart or under an effusion.

In 6 cases a different variety of track was observed. Associated in every case with an entry wound and bone damage at one end and a foreign body or exit wound at the other were found 2 roughly parallel linear shadows traversing the lung. In the 3 cases in which these could be viewed end-on an air-containing hole was seen. The presence of varying fluid levels in 4 of these cases and the marked resemblance of a tuberculous cavity in 1 suggested that air-containing missile tracks were present.

In length they vary from 4 to 10 cm. in width from 0.2 to 2 cm. Their walls may appear to be from 2 to 3 mm. thick or practically invisible; their caliber varies slightly along their course but on the whole they are digitate rather than fusiform. They tend to end abruptly about 1 or 2 cm. from the parietes or the foreign body. When viewed end-on they may appear rounded or oval and may resemble a tuberculous cavity or small lung abscesses. These cavities slowly heal by closing up from side to side over a period of weeks. The period during which they were under observation varied from eighteen to thirty-six days. There was no characteristic symptomatology. The significance of these lesions appears to be chiefly in the problem of their recognition and their differential diagnosis from a tuberculous lesion.

Extrapleural hematomas have been found around rib fractures, and in cases in which foreign bodies have come to rest in or just inside of the plane of the ribs. They consist of blood which has collected between the intercostal muscles on the one hand, and the parietal pleura on the other stripping of the pleura from the parietes results with its indentation into the lung parenchyma as the covering to a rounded hematoma. At operation the pleura has been found to be firmly adherent to the chest wall at the periphery of the lesion.

The roentgenological appearance is of a rather dense rounded shadow arising from the chest wall. It may arise gradually or steeply at its edges, and sometimes it overhangs at its lower border giving almost a pedunculated appearance. When viewed at right angles to the plane of its base it often has, especially when a week or two old a sharply defined border resembling a cyst. In size these lesions vary from 2 or 3 to 10 or 15 cm. in diameter. A lesion projected 7 cm. into the lung substance. They may occur anywhere over the chest wall but are usually visible only in the upper chest. In 4 cases there were four or more fluid levels and in 2 cases there were also small intrapleural effusions on the same side. The contents of these lesions may be fluid, clotted or infected blood and the gas they contain arises presumably from contact with the exterior or from gas-forming organisms. In 4 of the cases at operation a foreign body was found to be lying within the lesion's limits, with or without bone fragments from rib damage. These lesions slowly resolve over a period of weeks gradually subsiding to the chest wall, until they appear only as thickened pleura. The duration of this process is from four to eight weeks according to the size of the lesion. Such a process may become infected and if this occurs the area can be drained without involving the pleural cavity and the danger of empyema is thus avoided.

Lung contusion is a name given tentatively to the diffuse shadow found in so many traumatic chest cases when there is no evidence of pleural effusion to account for this change in density. It occurs in almost any type of lesion but is most striking in cases of chest wall injury when penetration of the pleura or parenchyma does not appear to have occurred. It may be associated with severe blows on the chest and with close up explosions, such as the detonation of cartridges carried in the patient's clothing without penetrating injury.

The etiology of this condition would appear to be similar to a blast effect. An early clouded appearance of the lung parenchyma is produced, which clears in the course of a few days occasionally the condition resembles an inflammation due to pleural effusion.

HAROLD C. OGDEN, M.D.

Rackow, A. M.: Some Problems of Appendix Radiology. *Brit. J. Radiol.* 944, 7 265

Roentgenography of the appendix is usually either neglected or abused. Although frequently the radiologist is called upon to render an opinion pertaining to the appendix actually little has been written concerning the roentgenographic appearance of the normal appendix.

The appendix can be visualized by a follow-through barium meal or barium enema, most authorities prefer the former. The mode of filling the appendix is passive but emptying is accomplished by contraction. In the past too much importance has been placed on the nonemptying of the appendix within twenty-four hours. Appendical barium retention may be caused by dehydration and caking of

the barium which produce concretions that are gradually expelled. A nonfilling appendix need not be due to pathology. It may be that during the examination period no barium was present nor had been expelled.

The author has adopted the following routine.

In the morning, a follow-through barium meal is given. From two to three hours later the patient is given 2 drachms of magnesium sulfate. The cathartic seems to stimulate appendiceal activity. Twelve hours later a second follow-through barium meal is given. It is probable that the second dose of barium will remain somewhat longer in the cecum after the effects of the magnesium sulfate have worn off and thus an opaque filling of the relaxed appendix will be provided. This method was successful in 76 per cent of the cases in which it was tried (25 of 33) as compared to success with one barium meal in 41 per cent (16 of 39).

The form and position of the appendix vary and the width of the lumen is variable. An indication of pathology is irregularity rather than total width. Segmentation may be due to local constrictions or to subdivisions of the barium caused by fecal particles. Neither is pathological. However if local constriction is constant it should be regarded with suspicion. A curled appendix may be due to a short meso-appendix. If the tip of the appendix is adherent to the iliopsoas muscle, pull on the cecum stretches the appendix and causes pain. Local tenderness may be deceiving because some physicians have an unconscious tendency to use more pressure when palpating over McBurney's point.

The author thinks that more attention should be paid by radiologists to appendiceal pathology. One way of learning more in this field could be realized by examining a series and establishing a normal criterion.

MAURICE D. SACKS, M.D.

Copleman, B.: The Roentgenographic Diagnosis of the Small Central Protruded Intervertebral Discs Including a Discussion of the Use of Pantopaque as a Myelographic Medium. *J. M. J. Radiol.* 944, 53 245.

The practice of the Neurosurgical Section of the Army Hospital with which the author is affiliated has been to request a myelographic examination in every case of suspected protruded intervertebral disc in which the lesion has been incident to Army service. As a result 150 cases were examined by means of myelography in slightly more than a year 86 of which were operated upon.

The many advantages of myelography are well known. In the author's series, however there are 5 cases in which very small midline protrusions of the intervertebral discs were detected by a most careful application of such a procedure and therefore their publication appears worth while.

The general technique of procedure is as follows.

The patient is placed in the lateral recumbent position as usually applied for lumbar puncture, on a roentgenographic-roentgenoscopic tilt table and,

after local anesthesia with novocain solution a lumbar puncture needle is inserted into the third or occasionally the second lumbar interspace. When a free flow of spinal fluid is obtained 3 cc of pantopaque are injected firmly and steadily so as to obtain a solid column of opaque medium. The stylet of the needle is then replaced and the patient turned slowly on his stomach. The table is now tilted and the advancing margin of the opaque column is watched for deformities until the third lumbar interspace is bridged. If slight persisting deformities are observed "spot" roentgenograms are made. The table is tilted still further and the fourth and fifth lumbosacral discs and the cul-de-sac are investigated roentgenoscopically and by spot roentgenograms. The column is then allowed to ascend the lumbar spine and additional careful studies are made. Finally the patient is turned into the prone position, the opaque column is maneuvered (by tilting the table) beneath the needle, and the opaque medium is withdrawn.

As a rule only the last three interspaces are examined but when the clinical examination indicates the upper segments of the spine are also investigated. The roentgenograms are made with the roentgenoscopic tube and a spot film device usually in the anteroposterior and moderately oblique views.

By following this procedure the author was able to discover in the 5 cases mentioned very small central disc protrusions whereas otherwise the condition might have been missed. It is important that in such cases the edge of the opaque column be allowed to advance slowly and gradually so that the outline of small protrusions be visualized before the bulk of the opaque substance obscures it. The 5 cases are briefly reviewed and their instructive roentgenograms reproduced. In all of the cases there was considerable pain which was completely relieved after removal of the protruding discs.

The author is of the opinion that the roentgen demonstration of these lesions was greatly facilitated by the use of pantopaque, a new opaque myelographic medium introduced during the past two years. The advantages of pantopaque are several. It is a freely flowing oily substance with less tendency to break up into globules than lipiodol. It casts an excellent shadow but does not obscure fine gradations of density and above all it is nontoxic. In all but 1 of the patients in whom the opaque material has been allowed to remain no ill effects of any kind were observed. The author cannot attest to the absorptibility of the drug since his longest observations started only six months ago but it is said that pantopaque absorbs slowly (about 1 cc. a year).

T. LEUCUTA, M.D.

Gianturco, C.: A Roentgen Analysis of the Motion of the Lower Lumbar Vertebrae in Normal Individuals and in Patients with Low Back Pain. *Am. J. Roentg.* 1944, 52: 261.

The normal movements of the spine are connected with several factors including muscular pull load upon the discs, intranuclear pressure and the condi-

tion of the articular facets. These factors vary with various segments of the spine and are altered by certain pathological conditions. It occurred to the author a little over a year ago that some advantage may be derived from a roentgen study of the pattern of motion of the various vertebral segments. With this view in mind he devised a method which permits such a study.

The method consists in the taking of 3 roentgenograms of the lumbosacral spine in the lateral position, one with the spine at rest, one with the spine in flexion and one with the spine in extension. The patient is placed in a special seat constructed by the author so that the pelvis is immobilized during the actual process of roentgenography. By superimposition of the sacrum in the 3 roentgenograms the shadows of the lower border of the fifth lumbar vertebra cross each in a definite manner. With the aid of an illuminator and sharp pointed pencil straight lines are drawn tangential to the lower contour of the fifth lumbar vertebra marking these shadows. The point of intersection of the line in straight erect position and the line in flexion represents the fulcrum of flexion of the fifth lumbar vertebra and the point of intersection of the line in straight erect position and the line in extension represents the fulcrum of extension of the fifth lumbar vertebra. The same procedure may be applied to the lines of the fourth and third lumbar vertebrae. So far no attempt has been made to extend the examination to segments above the third lumbar vertebra since a rather complicated device would be necessary for the taking of the roentgenograms above that level.

Obviously the terms fulcrum of flexion and fulcrum of extension although descriptive are not very accurate. The flat surface of the vertebral body as it slides over the turgid nuclear substance produces many intermediate points of crossing if roentgenograms in other degrees of flexion or extension are made. The points mentioned represent the two opposite extremes.

The author first applied the method to 20 normal individuals between the ages of nineteen and thirty-five years. In these with a normal pattern of motion the fulcrum of flexion and extension of the third, fourth and fifth lumbar discs were found to lie within very narrow limits at about the center of the nuclei. The average distance between the fulcrum was 5 mm with a minimum of 3 mm and a maximum of 8 mm. The fulcrum of flexion was always anterior to the fulcrum of extension.

Then he studied 35 patients with low back pain. Twenty of these patients showed normal pattern of motion but in 15 there was deviation from the normal. The exact distribution of the lesions in all cases is shown in Table I.

In attempting to explain abnormal vertebral motion the author discusses the importance of the muscular action, the effect of the bony lesions, the behavior of the posterior articulations of the spine and the influence of limited changes involving the

TABLE I — DISTRIBUTION OF LESIONS

Normal motion 30 cases (54%) without bone lesions, 6 cases, with bone lesions, 4 cases.		Abnormal motion 5 cases (46%) without bone lesions, 9 cases with bone lesions, 7 cases.	
Bone lesions found		Bone lesions found	
Cases		Cases	
Spondylolisthesis, grade		Spondylolisthesis, grade	1
Hypertrophic changes		Hypertrophic changes	1
Schmorl's nodes	1	Osteochondritis juvenilis	
		Old compression fracture	
		Unilateral sacralization of the fifth lumbar	

intervertebral discs. It is fully realized that a great deal of investigation will be necessary to establish the exact anatomical basis for the various types of abnormal motion.

The fact that in a high percentage of patients with low back pain abnormal vertebral motion was found is significant. It is hoped that this will stimulate further research.

T LUCOTIA, M.D.

Rhodes, A. W. and Borrelli, F. J.: Giant Hemangio-endothelioma with Thrombocytopenic Purpura. *Am J Roentg* 944, 52-53.

Giant hemangioendothelioma with thrombocytopenic purpura is a rare entity. The literature reveals the report of only one other case.

In the present case, a tumor of the back and neck was noted at birth (November, 1941) and diagnosed as lipoma. Two months later it began to increase in size with a blue discoloration. The tumor blanched on pressure. Petechiae and small areas of ecchymosis were present throughout the body. The tumor continued to increase in size and the patient was admitted to the hospital, vitamin K and multiple transfusions were given. In addition 220 roentgens were given in one dose with 150 kv and 1 mm. of aluminum filter at 25 cm. distance with no effect. The mass continued to increase in size and extended to the left side of the face and chin involving the entire left thoracic wall. Hemorrhagic spots were noted around the base of the tongue, soft palate, fauces, and pharynx. The spleen was palpable. The hemoglobin was 9.2 gm. the red blood cells numbered 3 million, the white blood cells 15,500 and the platelets 15,000 the coagulation time was four minutes and the bleeding time twenty five minutes. Roentgenograms revealed a soft tissue tumor of the chest and neck but no evidence of bone destruction.

On May 4, the patient became critically ill following an upper respiratory infection. Two courses of radiation therapy were given. The first course was given over a period of three weeks (from May 8 to June 1) and consisted of 10 treatments, 100 roentgens per treatment, 4 portals, from 7 by 7 cm. to 1 by 10 cm. 140 kv, 3 mm. of aluminum filtration at 5 cm. tube-skin distance. Three hundred roentgens were given to the left lateral neck, 300 roentgens

to the left shoulder (lateral port) 300 roentgens to the left shoulder (anteroposterior port) and 300 roentgens to the left shoulder (posteroanterior port). A slight change was noted and two weeks later a second course was given 300 roentgens to each of the three ports. In August, a third course of irradiation was given 160 kv 25 cm. distance, open field inherent filtration of 0.15 mm. of copper 275 roentgens to the shoulder (posteroanterior field). The same dose was repeated two days and two weeks later with a 20 by 20 cm. field at 50 cm. distance and on October 23 275 roentgens were again given with a 20 by 10 cm. field.

Response to radiation therapy was gratifying. Within two months, the mass regressed in size and the discoloration faded slowly. Biopsy report of the lesion was hemangioendothelioma. Observation one year later revealed that most of the skin looked normal except for a slight purplish discoloration of the arm due to recent bleeding, and the shoulder skin was roughened and red. Both areas were given a single dose of 275 roentgens. The bleeding time was four and one-half minutes and the clotting time one and one-half minutes. The platelets numbered 450,000 per cubic millimeter. When last seen, the purple areas had disappeared and the child was developing normally.

The authors raise one very pertinent point concerning the efficacy of radiation therapy. The involved fields were extensive undoubtedly the irradiation of the ribs and spleen underlying the tumor helped not only in the regression of the tumor but also in the elevation of the platelet count, which resulted in a lowering of the bleeding time and disappearance of the purpura.

MAURICE D. SACKS, M.D.

Cantril, S. T., and Buschke, F.: Roentgen Therapy in Gas-Bacillus Infection. Report of 9 Cases with Recovery. *Radiology* 944, 431-433.

There appears to be considerable difference of opinion regarding the efficacy of irradiation in the treatment of gas gangrene. Opponents of this type of treatment state that animal experimentation has not been successful. Recently however Merritt described experimental gas gangrene in sheep, and it is the authors' belief that this report should answer the critics.

Nine cases of gas gangrene are reported in detail. The final results clearly demonstrate that x-ray therapy alone or in conjunction with surgery is very effective in the management of gas gangrene. (Emphasis is placed on the individuality of each case regarding surgery and irradiation.)

All 9 of these cases of gas-bacillus infection were due to trauma. Although there was no mortality in the series the authors believe that it may not always be possible to maintain so low a mortality rate. They further believe that in all probability the long-term mortality rate will be similar to that of Kelly (1.2 per cent). Without doubt, a mortality of from 10 to 15 per cent is a very marked saving in lives.

Because of the extent of the trauma amputation was necessary in 4 of the cases in 3 of the 4 cases x-ray therapy served to limit the infection and reduce toxemia and the patients became better surgical risks for amputation. In the fourth instance although the extent of trauma made immediate amputation unequivocal there was a reduction in toxemia.

Four other patients received therapeutic doses of antitoxin. One had a severe serum reaction. The authors are of the opinion that these patients would have recovered regardless of whether or not the antitoxin had been used. Sulfonamides were effectively used in 2 cases with secondary bacterial infection after the gas-bacillus infection was under control and x ray therapy had been discontinued. Chemotherapy was used in several other cases but the authors are convinced that this did not help in controlling the actual progress of the disease other than to combat secondary bacterial infection.

The authors conclude that the mortality from gas gangrene, whether in civilian or military life can be minimized by thoughtful diligent use of both surgery and roentgen ray therapy.

MAURICE D. SACHS, M.D.

MISCELLANEOUS

Alexander T. C.: Irradiation Pneumonitis. Report of a Case. *Bull Johns Hopkins Hosp.* 1944 75 199.

The author reports a case of Hodgkin's disease in which the patient died from pneumonitis as a result of overirradiation of the mediastinum and unprotected lungs.

The patient was treated from January to September 1939 and he died on September 28 1939. During this period he received the following amount of radiation over the mediastinum and adjacent lungs from January 21 to March 1 a dose of 1 050 roentgens in air given in 10 fractions through a field 10 by 20 cm. over the mediastinum anteriorly and a similar dose posteriorly from April 26 to May 4 a dose of 420 roentgens in air given in 4 fractions through a field 10 by 20 cm. over the mediastinum anteriorly and a similar dose posteriorly from July 31 to August 17 a dose of 2 018 roentgens in air given in 10 fractions through a field 15 by 15 cm. over the mediastinum posteriorly and a dose of 1 818 roentgens given in 9 fractions through a field 20 by 20 cm. over the mediastinum anteriorly and, finally from September 22 to September 28 a dose of 243 roentgens in air given in 3 fractions through a field 20 by 20 cm. over the mediastinum posteriorly. Thus during eight months a total of 7,019 roentgens in air was administered to the mediastinum through fields as described without any provision for shielding the lungs. The factors employed were 200 kv p 20 ma. 50 cm. skin target distance, Thoracul filter 2 mm. of copper plus 1 mm. of aluminum.

The patient developed severe respiratory embarrassment with progressive cyanosis in the terminal stage and a roentgenogram eight days prior to his death revealed an extensive pneumonitis. Post mortem examination showed pulmonary changes which were similar to those produced by overirradiation in experimental animals by Davis and described later by McIntosh and Spitz and by Warren and Spencer. No evidence of Hodgkin's tissue was found in the lung tissues.

T. LEUCUTIA, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Ladell, W. S., Waterlow J. C. and Hudson, M. F.: Desert Climate; Physiological and Clinical Observations. *Lancet* Lond., 1944, 247, 491

Heat exhaustion of type 2 was seen almost exclusively in the second half of the summer. The incidence seems to be related not to the height of the temperature but to the duration of the hot weather. The most prominent symptom was defective sweating which was a complaint in 37 per cent of the cases. The duration of this symptom was short in some cases and as long as three weeks in others. A common symptom in this type of case was dyspnea, which was present in 23 of 55 cases, and was associated with numbness and tingling of the hands and feet in 8. Dyspnea and exhaustion were worse in the middle of the day. Often the subject felt fairly well in the early morning but symptoms began to come on at about 11 a.m. Vomiting and cramps were present in only 2 cases and were not severe. Increased frequency of urination was extremely common. Several patients said that the frequency started when sweating began to be defective. These patients did not look ill. There was slight tachycardia on admission. The pulse volume was also good. The mean systolic pressure lying down was 121 mm Hg which is nearly 20 mm. higher than the mean in controls at the same time of year. The diastolic pressure was quite variable with a mean of 69 mm. Hg. Many patients showed obvious and easily elicited capillary pulsation in the nail bed. The reaction to standing was normal. High temperatures are not found and this is one of the features that differentiates this group from hyperpyrexial cases. Eighty per cent of the patients of this type had had severe or moderately severe prickly heat and this was characteristically in the scaling stage. The outstanding chemical feature of these cases was the excretion of large volumes of dilute urine. The greatest volumes of urine were recorded toward the end of the season. The only abnormalities found in the blood were reduced whole blood chloride and reduced plasma chloride. Blood urea levels were low.

All patients were encouraged to drink larger amounts of fluid. Salt by mouth in doses of 35 to 1 ounce were given to alternate cases. Progress in objective signs was slow. The average blood pressure on discharge was identical with that on admission. The low diastolic pressure and high pulse pressure noted in some cases often persisted for many days. The urine output remained high. The average weight gain in these patients during their stay in the hospital was 41 ounces which was significantly less than the average gain of 121 ounces in those with heat exhaustion of type 1. Extra salt

by mouth did not have any effect upon the amount or rate of gain in weight.

HAROLD C. OCTAVIAN, M.D.

Ladell, W. S., Waterlow J. C. and Hudson, M. F.: Desert Climate; Physiological and Clinical Observations. *Lancet* Lond., 1944, 247, 517

An outline is made of observations in Shaiba in southern Iraq on British Army personnel during the summer of 1943. Maximum temperatures above 100 F occurred daily for four months and there were two periods, one of a week and the other of a fortnight, when the temperature each day was above 115 F. The humidity was low and the climate was thus a true desert climate. Observations were made on 24 soldiers. The pulse rate of the subjects lying down remained constant throughout the summer at an average level of 65. At the beginning of the summer, the average blood pressure taken on subjects lying down was 112/72 mm. Hg. As the weather became hotter the blood pressure gradually fell to a minimum of 97/62. Thereafter it rose again but by the end of October it had not reached the initial level found in May. All the subjects lost weight in the hot weather and some of them lost as much as 7 per cent of their initial body weight. When the weather became cooler they recovered weight. The volume of urine passed in twenty-four hours also fell as the weather got hotter. A low urine output was associated with a high blood urea. Dehydration was most probably the result of the insufficient intake of salt. It was found that those subjects who lost most weight had the greatest chloride concentration in their sweat. These observations suggest that there are certain individuals who have a higher salt requirement than the average. They react to high rates of sweating by cutting down salt loss in the urine to a minimum. The chloride content of the body fluid is kept up by a reduction in the total fluid volume shown by the loss in body weight.

Hyperpyrexia. Twelve patients were seen who had a rectal temperature of 107 F or more. Of these 12, 9 were over thirty years of age compared with 40 per cent over thirty in the whole series. Five of these cases occurred during the hottest week of the summer.

In most patients the onset was sudden. All except 1 gave a history that sweating stopped over a period varying from twenty-three days to half an hour before the attack. The main elements in the clinical findings were rectal temperature of 107 or more, a skin hot and dry to the touch all over the body and partial or complete loss of consciousness. Abdominal and tendon reflexes were absent in only 3 cases. Blood samples showed diminished hemoglobin and a chloride content in both the whole blood and the plasma which was slightly less than normal. The

blood-urea and plasma levels were within the limits found for controls. The sodium content estimated on 2 samples only was also normal. Although there was some chloride deficiency in the blood there was an apparent anomaly in that all these cases had chloride in the urine. Treatment was along established lines. The body temperature was reduced with wet sheets and fanning of the patients who were then transferred to an air-conditioned ward with a temperature of about 80° F. Losses from rapid sweating were restored within twelve hours of the onset in most cases.

The laboratory findings fit in with the theory that the first breakdown is in the sweating mechanism. Recovery was rapid and uneventful.

Heat exhaustion type 1. The great majority of this type of cases were seen in the two hottest weeks of the summer. The history was usually short, from two to four days. Complaints of dizziness, anorexia, headache, and constipation were present in varying combinations. Vomiting and cramps were prominent symptoms, cramps usually preceded the vomiting. Most of these cases had no history of diminished sweating or of increased frequency of urination. On admission the patients looked exhausted, anxious and ill. They were pale and sweating profusely with a cool skin. They showed the classical signs of dehydration.

The average rectal temperature was 100.6° F. The average pulse rate on admission was 90 in 35 per cent the pulse volume was poor. In patients lying down, the systolic pressure was occasionally low but the diastolic pressure in most cases was higher than in the controls.

In the first twenty four hours after admission the patients passed relatively little urine and this was heavily pigmented; the specific gravity was often over 1.020. Intravenous administration of saline solution and fluids given by mouth increased the urine volumes. A raised hemoglobin and plasma protein content indicated hemoconcentration. The chloride content of the whole blood and that of the plasma were both grossly diminished; the drop in chloride of the whole blood was more marked than that in chloride of the plasma. The blood urea was raised in all cases.

In all cases liberal fluids by mouth were ordered. Some patients were given extra salt by mouth in daily doses of 1 ounce. Those who were dehydrated or could not retain fluids received intravenous saline solution usually from 4 to 5 pints in three hours. Most of the patients responded rapidly to treatment.

The evidence points to a salt deficiency dehydration as the cause of type 1 heat exhaustion. This develops when sweating rates are high in individuals who habitually excrete an unusually high concentration of chloride in their sweat. It can be prevented by drinking enough to keep the urine output at least at 30 ounces a day and by the administration of 48 gm. of sodium chloride daily. The personnel should be weighed at regular intervals during the hot

weather and any man who shows a persistent loss of body weight should be instructed to drink more water and take more salt.

HAROLD C. OCHSNER, M.D.

Elkinton J. R. and Winkler A. W. Physiological Effects of Drinking Undiluted Sea Water. *War Med. Chir.* 1944, 6: 241.

Recent clinical and experimental observations indicating the cause of the deleterious effects of drinking undiluted sea water are presented. In composition sea water closely resembles vertebrate extracellular fluid except that its total ionic concentration is about four times as great. In view of the fact that indefinitely large amounts of sea water can be ingested if sufficiently diluted with fresh water, it would appear that the deleterious effects of drinking undiluted sea water are related to its hypertonicity. Since the highest recorded concentration of sodium as sodium chloride in human urine does not exceed 19 per cent the ingestion of undiluted sea water presents a dilemma to the organism. Either some of the ingested sodium chloride must fail of excretion or body water must be sacrificed to eliminate the salt. Magnesium and sulfate require even more water per mol for their excretion than sodium chloride since the former ions are excreted in isotonic concentration by the intestine.

The actual response of the organism to drinking undiluted sea water will depend on many factors including the state of hydration of the body and the rate of ingestion of the sea water. In any event hypertonicity of the body fluids must result. The character of the hypertonicity however depends on whether or not salt is retained. With no retention of sodium chloride, loss of fluid is distributed over both extracellular and intracellular compartments in proportion to their initial magnitudes. On the other hand any retained sodium or chloride is confined to the extracellular phase of the tissues with a resultant osmotic shift of water from the cells to the extracellular fluid.

Experiments done on human subjects are necessarily confined to the early stages of the effects of ingestion of hypertonic saline solution. The later and more severe physiological effects were studied in dogs. Both acute and chronic experiments were included. Since dogs can produce urine that is more concentrated than that of human beings it was necessary to give the dogs a 5 per cent saline solution as compared to a 3.5 per cent solution for human beings in order to produce an analogous condition. The experiments illustrate clearly an important difference between the earlier and later distribution of the dehydration which results from the persistent ingestion of hypertonic saline solution. Complete excretion of salt may be attained at first with presumably the same proportion of depletion for both the extracellular and intracellular phases. As dehydration progresses body water is not so readily sacrificed and some sodium chloride is retained which results in excessive depletion of the intracellular fluid.

to maintain the extracellular concentration. The extracellular volume was fairly well maintained in spite of progressive total dehydration. The urinary concentration of salt gradually rose but did not reach the level of the concentration of salt in the solution ingested. Shortly before their death the animals exhibited various disturbances of the central nervous system including tremors, hyperactive reflexes, motor inco-ordination, and finally irregular and falling respiration. The circulation in the meanwhile continued to function well. There was no collapse of the plasma volume, renal excretion remained active, the pulse was vigorous and the electrocardiograms were normal. The terminal event was respiratory failure and the picture was clearly not one of circulatory failure.

From a practical standpoint there would appear to be no advantage to castaways in the drinking of diluted sea water instead of ingesting the diluent alone. With respect to the suggestion that water requirements might be met, as in seals, by the ingestion of fluids from the flesh of fish, the authors state that this is reasonable from the standpoint of salt excretion, but it ignores the fact that much urea, requiring water for its excretion, is formed from the protein which is in the fish.

JOHN L. LINQUIST, M.D.

Altman, R.: The Prophylaxis of Cutaneous Cancer. *Edinburgh M J* 1944, 5: 339.

Cancer is a disease which is increasing in importance in view of the amount of attention which has been directed to it and the misery and suffering which it brings so often in its train. It has frequently been asserted that the incidence of cancer is greater than formerly. This view however has been questioned those who oppose it maintaining that the increase is to a large extent due to the fact that it is readily recognized now whereas formerly it escaped observation. It is interesting in this connection to study the figures of cancer as seen in the Skin Department of the Royal Infirmary in relation to the number of out-patients attending.

These figures show that the percentage increase of cancer of the skin in recent years is negligible. There has been rather more than a 40 per cent increase in the number of new patients attending the Skin Department during the last ten years while the increase in the cases of skin cancer has been 0.11 per cent.

One point has to be kept in mind in studying these figures. In the author's opinion more cases of rodent ulcer at an early stage are being sent up to the Skin Department than formerly. It being not uncommon now for rodents the size of a lentil or less to be referred for treatment.

Another point to be noted is the small number of cases of squamous-cell cancer. An average of just over 3 per annum has been seen against an average of 90 rodents. Thus the squamous-cell carcinoma forms a very small percentage of the total cancer cases.

It might be thought that the skin is an excellent organ for studying the problem of cancer and in some respects this is true. We are however faced with the difficulty that we know so little of the cause of cancer of the skin. It is true that certain substances are prone to produce cancer but that does not take us far. These carcinogenic substances, as they are called, produce only one type of cancer and that is the less common squamous-cell variety. No such substances can be blamed for producing the rodent ulcer type which, as is seen from the figures given, is much the more common. About the cause of this type we must confess ignorance, and so no prophylactic measures can be taken. The relationship of injury to cancer is not clear. This is true of cancer of the skin as well as of cancer of other organs. It is unusual to obtain any history of injury in cases of rodent ulcer.

The substances which produce cancer are many and varied. Most of these are external irritants but there is one drug which when taken internally over a prolonged period, tends to give rise to squamous epithelioma. This drug is arsenic. Prolonged ingestion of arsenic gives rise to hyperkeratosis of the palms and soles, and eventually some of these hyperkeratotic areas become malignant.

Many physical and chemical agents produce cancer of the skin. The most notable are light, heat, and x rays among the physical and soot, tar, pitch, anthracene and paraffin among the chemical. It is probable that a particular type of skin, inherited or acquired, is necessary for the development of cancer as it is only a small proportion of persons coming in contact with these substances who develop the cancerous condition.

Most of the other substances which ordinarily produce carcinoma are met with in the course of working with them, the condition thus becoming an occupational hazard. Soot is known to be provocative of cancer and it was the first product of coal distillation known to produce injury. Potts described chimney-sweepers' cancer which occurs on the scrotum and it is curious that this form of the disease seems to occur according to Pusey only in England.

Tar and pitch are other substances which produce skin cancer. According to Prosser White, lignite, gas-works tar, producer gas tar and coke-oven tar will give rise to epithelioma, while blast-furnace tar does not either in men or mice. It would seem that it is the fractions which distill at a high temperature which cause epithelioma, and the critical temperature seems to be about 350° C. In the Skin Department many patients are treated each year with crude coal tar and there has not been a case recorded in which the patient developed cancer as the result. Not one of the cases of squamous-cell carcinoma occurring in the ten year period mentioned earlier had had any tar treatment, nor so far as the author is aware has any of the numerous patients who received treatment with crude-coal tar ever developed carcinoma of the skin as a result.

Another industry in which cancer has been common is the cotton industry. Here the mule spinners are those chiefly affected. It may occur on the arms but the scrotum is the place usually associated with epithelioma in this industry. The oil from the spindles is thrown out as they rapidly rotate and the workmen's clothing becomes saturated with it. Friction of the scrotum against the mule frame as the worker leans forward is the other factor concerned. Women who work in this department are not affected.

About 70 per cent of all cancers seen in mule spinners are on the scrotum. It is strange but it would appear that no cases of this particular cancer have been reported in France, Germany, Russia, or Poland while it seems to be rare in the United States.

The true paraffin cancer arises in workers in the paraffin department of the shale oil industry. Various earlier lesions occur sometimes within a few weeks after the worker is employed in this department.

The lesions disappear in a short time if the employee ceases to work with paraffin but they persist in greater or lesser degree as long as the men continue to work in the department. The early lesions may be comedones but much more common is an inflammation of the mouths of the follicles. This is the characteristic shagreen skin which occurs not only in paraffin workers but also in mule-spinners and the author has also seen it in a worker in a ropery where mineral oil was used. One other feature completes the picture and that is the presence of warty lesions. The important point about this lesion is that it may develop many years after the worker has ceased to be employed in the paraffin department. These warts are the precursors of carcinoma though it may also arise from indurated papules.

With regard to the actual cause of the carcinoma it is definitely established that it consists in the contact with the oily paraffin scale as the scale itself has been proved not to be the cause. The oil is the agent which provokes the changes in the skin which eventually lead to the cancer.

The prophylactic measures adopted at the Scottish Oil Works have been efficient and successful. Each man has a bath after quitting his work. Soiled working clothes are put into lockers which are heated and are thus dry before the men resume work next day. A rigorous selection of the men employed in the paraffin department is made all showing an early tendency to paraffin eruptions being removed and sent to other departments.

What has been done in this industry may be done in others. Admittedly the number of men employed in the paraffin department of Scottish Oils is not large, but mere numbers should not be allowed to stand in the way of measures designed to prevent such a serious industrial hazard. The willing cooperation of employers, employees and medical men is essential to the success of such a scheme.

JOHN F. KIRKPATRICK, M.D.

Butler A. M. and Talbot N. B.: Medical Progress: Parenteral Fluid Therapy. Estimation and Provision of Daily Maintenance Requirements. *V. England J. M.* 1944, 331-385.

The last fifty years have witnessed a steady increase in knowledge concerning the metabolic disturbances resulting from starvation and dehydration. In addition, the increased availability of specific nutrients and of solutions through parenteral administration has increased not only the possible effectiveness of parenteral nutrition and repair therapy but also the physician's responsibility in the parenteral administration of fluids. This review presents in outline form such basic data as may be helpful in effectively utilizing this knowledge in the parenteral therapy that is at hand today or may become available tomorrow.

Tables 1, 2, and 3 best present these basic facts.

As to the manner and rate of parenteral administration, the authors state that since information regarding many factors concerned with optimal utilization of such nutrients is lacking, the prescription of the rate of infusion and composition of parenteral fluids for a given patient must reflect common sense.

TABLE 1—APPROXIMATE NORMAL SODIUM CHLORIDE MAINTENANCE ALLOWANCES PER DAY FOR RESTING NONSWEATING PERSONS OF VARYING SIZE

Size	Sodium Chloride	Physiological Saline Solution
	gm.	cc.
Infants		5
Children	5	350
Adolescents and adults	6	700

TABLE 2—APPROXIMATE DAILY CALORIC REQUIREMENTS OF NORMAL RESTING PERSONS OF VARYING SIZE, TOGETHER WITH THE DAILY DEXTROSE AND AMINO ACID ALLOWANCES* THAT THEORETICALLY MIGHT SATISFY THEM

Size	Daily Caloric Requirement	Daily Dextrose Allowance		Daily Amino Acid Allowance	
	al. 2 gm.	gm./kgm.	cal./kgm.	gm./kgm.	al./kgm.
Young infants	60	6	54	5	6
Old infants	33	5	5		4
Children	5	7	8	6	
Adolescent and adult	5			6	

* A solution does not suggest 5 gm. of amino acid 100 cc. of solution should allow for the adult but for estimating the daily allowance for the younger (less) best on high carbohydrate diet is average.

TABLE 5—APPROXIMATE NORMAL WATER LOSSES AND ALLOWANCES PER DAY FOR PERSONS OF VARYING SIZE NOT SUBJECT TO EXERTION OR SWEATING

Size	Water Loss				Usual Water Allowances		
	Urine	Stool	Insensible	Total	cc/person	cc/kgm	oz/lb
	cc	cc	cc	cc	cc/person	cc/kgm	oz/lb
Infant (to 10 kgm)	200-300	5-20	15-300†	300-320	120-1800	65-100	2-4
Child (to 40 kgm)	300-800	20-100	300-600	620-1400	600-1800	100-45	3-6
Adolescent or adult (60 kgm)	800-1000	00	600-1000†	1400-2000	800-2000	45-70	3-6

† Including the water content and loss of oxidation of food, which under normal circumstances, except for infants, approximates the insensible water loss.

‡ 3 cc per kilogram per hour
to 5 cc per kilogram per hour

careful clinical observation, and a "tolerance" indicative of an enlightened awareness of ignorance.

J M MORA MD

DUCTLESS GLANDS

Finkler R. S. Furst N. J. and Klein M. A. Clinical and Roentgenological Study of the Effects of Hormonal Therapy on Bone Growth. *Radiology* 94:4, 43-54

Observations on the rate of bone growth were made not only on children treated for growth deficiency but also on those showing hypogenitalism, cryptorchidism, pseudo-Froehlich's syndrome, obesity and mental retardation. Clinical observations of growth and of genital and somatic development were recorded prior to and during, and after therapy routine roentgen studies of the skull, sella turcica and long bones were made at regular intervals. The skeletal age was estimated by the epiphyseal development of the distal ends of the radius ulna, metacarpals and the phalanges of the hands, by the presence of the centers of ossification and the number of carpal bones. The progress of skeletal development was judged in accordance with the standards of Todd. The degree of mineralization was estimated by the standards established for the study of osseous structures.

These studies were carried out on a group of 81 children of whom 65 were clinic patients and 16, private patients. The therapeutic agents employed were thyroid substances (in 18 children), extract of the anterior lobe of the pituitary gland (in 36 children), chorionic gonadotropin (in 10 children), and male sex hormone (in 18 children). The effect of the various hormones on skeletal growth, bone density and epiphyseal union was noted.

Before hormonal therapy all of the children presented various psychological maladjustments most of them were shy, self-conscious, and unsocial. Others were resentful toward their parents, guardians or society in general. Following successful endocrine therapy with improvement in growth and genital and muscular development there was a tendency to improvement in mental and emotional stability.

EARL C. ROSENTHAL, M.D.

Glute, H. M. and Williams, R. H. Thiouracil in the Preparation of Thyrotoxic Patients for Surgery. *Ann. Surg.* 1944, 120: 504.

The authors report their experience with thiouracil in 115 thyrotoxic patients. 81 of whom were treated without surgery, the remaining 34 were treated with thiouracil and surgery. The medically treated patients experienced, for the most part, an early return to normal without further toxic manifestations unless iodine had been taken for a long time previously.

Of the 34 surgical patients, 4 had toxic adenomatous goiter, the others had typical uncomplicated exophthalmic goiter. Surgical patients were treated for 6 to 8 weeks preceding thyroidectomy, were usually operated upon after two days of hospitalization, and returned home six or seven days after operation.

Certain patients, perhaps 10 per cent, have complications from thiouracil of sufficient degree to necessitate discontinuation of the drug. The most serious complication are agranulocytosis, leukopenia, morbilliform rash with itching, and nausea and vomiting.

During the period of preoperative preparation, usually the thyroid gland became smaller and firmer. The active pulsations, thrills and bruits tended to disappear. In some cases, however, the goiter seemed to become larger as treatment progressed but this was unusual. In most patients having a stare and a widened palpebral fissure, improvement in the eyes occurred as their general condition improved. In individuals showing manifestations of malignant exophthalmos, apparently the minimal effective dose of thiouracil should be used to bring the metabolism to normal. Over-treatment may lead to an increase in the exophthalmos.

At the time of operation the thyroid gland in thiouracil treated patients is firm and resembles the consistency of the untreated hyperplastic thyroid. It is not as vascular as in untreated patients, although the superior and inferior arteries are still of large caliber. The tissue surrounding the gland is at times densely adherent to it and cleavage planes are hard to establish. More bleeding is encountered in some of the thiouracil-treated patients than in the iodine treated patients.

Histologically the thiouracil treated hyperplastic gland showed very little colloid. The cells of the acini were tall and columnar. Many of the acini were small and contracted, only a few showing papillary projections. There seemed to be an increase in interstitial tissue between the acini. There was little histological difference between the glands of patients treated only a few weeks and the glands of patients treated over a period of many months. In patients who received both iodine and thiouracil there were definite increases in the colloid contents of the acini as compared to the findings in patients who had received no iodine.

The operative course in thyrotoxic patients treated for five or six weeks with thiouracil is characterized by its smoothness. Like patients with a normal metabolism, these patients react to a moderate surgical procedure with no outstanding changes in the pulse or blood pressure and with a postoperative course that is smooth and uneventful. The nervousness, activation and severe tachycardia were entirely absent in the authors' cases. The induction and maintenance of anesthesia are the same as in any patient with a normal metabolism. Cyclopropane-oxygen has been the anesthetic of choice in all of the authors' patients.

STEPHEN A. ZIEGLER, M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Wills, R. A.: The Mode of Origin of Tumors. Solitary Localized Squamous-Cell Growths of the Skin. *Cancer Res.*, 1944, 4: 630.

The most prevalent view concerning the mode of origin of tumors is that each tumor has a simple unicentric origin arising at a single point in time from a single small focus of cells and that it enlarges only by multiplication of these cells and their descendants.

To test this theory the author studied the structure of 10 early localized, solitary squamous-cell carcinomas of human skin, and came to the conclusion that the structure of these growths was incompatible with a strict unicentric view regarding their origin, and that, instead, the structure showed that each has arisen by spreading cancerization of a field of epidermis.

The precancerous state of an area of skin includes significant dermal changes, especially in the subepithelial elastic tissue, and invasion of the dermis by the cancerous epithelium probably commences at points of greatest damage to the dermal elastic.

Progressive neoplasia in a field of tissue does not imply the passage of any carcinogenic stimulus from cell to cell, but is merely the progressive response of an area of epithelium to the same original stimuli, the timing and distribution of this progressive response depending on the distribution and intensity gradients of the causative stimuli.

The author believes that the evidence advanced justifies the view that squamous-cell carcinomas of the human skin are comparable with those produced

experimentally and that they are the products of the following sequence of events:

- 1 A skin field more or less extensive, has been subjected to a succession of carcinogenic stimuli (still often unascertainable in human beings) which have induced slow progressive changes in both the epidermis and dermis of that field and are structurally apparent as precancerous hyperplasia.

- 2 At the central focus (or at several high potential foci) of the field, hyperplasia passes into irreversible neoplasia, with or without immediate invasion of the dermis by the epithelium.

- 3 As cancerous proliferation and invasion progress at the central part of the field, cancerous change of the surrounding unstable epidermis takes place in a steadily enlarging area around the center.

- 4 After the entire field of the predisposed epithelium has become cancerous the tumor enlarges solely by proliferation of the cancerous cells and structural evidence of its mode of origin is soon lost.

The author strongly emphasizes the point that a skin cancer in its early formative stage arises more by a gradual transformation of pre-existing epidermis than by cellular multiplication and that only after the formative field has all suffered neoplastic change does the tumor grow solely by multiplication.

JOSEPH K. NABAT, M.D.

Berenblum, I.: Irritation and Carcinogenesis. *Arch. Path., Chic.*, 1944, 38: 233.

In this review the author carefully defines his terms and poses a series of questions which he answers by logical reasoning and by known clinical and experimental evidence in an attempt to arrive at the relationship between irritation and carcinogenesis.

The first question presents the problem in its crudest form: Are all irritants potentially carcinogenic? An affirmative answer would mean that irritation plays an essential part in the production of tumors while an answer in the negative would mean that irritation is not by itself responsible for tumor formation although it might play a vital part in carcinogenesis. With certain physical agents designated by the term "radiation," including roentgen rays, gamma rays, and ultraviolet rays, there is an apparent correlation between their power of producing injury to tissue and their ability to induce tumors. Of many chemical irritants tested only a small proportion have been found to possess carcinogenic action. Trauma in the sense of one or a few mechanical injuries cannot be accepted as an important or frequent cause of tumor formation in view of the extreme frequency of traumatization and the extreme rarity of tumors of proved traumatic origin. In regard to a relationship between long continued friction and tumor formation, the operation of other factors sometimes makes the answer difficult, but chronic mechanical irritation (friction) cannot be accepted as a common or even likely cause of tumor formation. The relation of thermal injuries to carcinogenesis is complicated by the fact that they do not represent a single entity but the available

evidence is more convincing than that concerning mechanical injuries. Both burns and repeated freezing have been demonstrated to be carcinogenic. Other experiments do not support the view that irritation itself is a deciding factor in carcinogenesis and, thus, the answer to the question "Are all irritants potentially carcinogenic?" is emphatically No.

The second question is "Are all carcinogenic agent irritants?" This question requires a definition of what is meant by irritant. If by "irritation" is meant the production of a continued state of reparative hyperplasia which is the meaning as defined in this review then all the direct carcinogens, without exception, are irritants. One is thus brought back to the central problem of hyperplasia. What does it represent? How does it differ from neoplasia? And what evidence is there that preneoplastic hyperplasia is biologically different from reparative hyperplasia? Hyperplasia and neoplasia are both cellular proliferation in excess of the normal. The distinction lies in the extent or limit of growth. Knowledge of the development of occupational tumors in man and experimentally induced tumors in animals points to the occurrence of a preneoplastic hyperplasia preceding the development of a tumor. The conclusion already reached that all direct carcinogens are irritants means when translated into terms of response that all tumor-producing agents are also hyperplasia-producing agents. These facts taken together indicate that hyperplasia is an invariable and essential preliminary to neoplasia. But it has already been shown that not all irritants are carcinogenic. Therefore, preneoplastic hyperplasia must be a special kind of hyperplasia biologically distinguishable from ordinary reparative hyperplasia. Further the experimental evidence that preneoplastic hyperplasia is of a specific type is convincing.

It is conceivable that the development of a tumor out of normal tissue could be a sudden change or it could be dependent on a sequence of separate specific biological reactions. In the neoplastic transformation of the skin of the mouse or rabbit following application of a carcinogen, three distinct phases can be recognized: (1) the prewart stage during which hyperplasia is the dominant lesion, (2) the stage of benign tumor growth during which one or more papillomatous structures appear and grow and (3) the stage of cancer when one of the latter structures starts to infiltrate the subepithelial tissues. The question arises as to whether the three phases are consecutive stages of a single carcinogenic process, or are they consecutive but separate processes? Several methods of approach have been used in an attempt to answer this question. The balance of evidence is in favor of the view that prior to the establishment of cancer continued stimulation enhances the carcinogenic process. The experimental data are tabulated in three groups of results: (1) the irritant and the carcinogen are applied concurrently, (2) the irritant is applied for a period preceding the application of the carcinogen and (3) the irritant is

applied after the application of the carcinogen has been discontinued.

The effect of applying another irritant concurrently with a carcinogen varies according to the irritant used, but most irritants seem to have no significant influence when applied in this way. This is further evidence that intensity of irritation is not the deciding factor in carcinogenesis. These experiments bring to light the existence of specific cocarcinogenic agents and equally specific anticarcinogenic agents. More precise information is derived from experiments in which the application of the irritant either precedes or follows the treatment with carcinogen. Ordinary irritants generally prove unsuccessful in producing a preneoplastic lesion of the skin, but many of them seem able to precipitate a tumor once the preneoplastic state has been established. The balance of evidence is therefore strongly in favor of the view that the component phases of carcinogenesis are consecutive but independent processes.

Thus the evidence indicates that preneoplastic hyperplasia is a highly specific type of hyperplasia since only carcinogenic agents can produce it with certainty but that once the preneoplastic stage has been induced by a true carcinogen a benign tumor can be made to appear at that site and a tumor already present can hasten its progress to carcinoma by the action of a variety of noncarcinogenic irritants. If this is confirmed the following practical lessons will have been learned: (a) there is little danger that an ordinary irritant will produce a tumor of its own accord, (b) this applies also to the initiation of a preneoplastic lesion and (c) given a preneoplastic lesion the subsequent development of a benign tumor at the site may be facilitated, and its progress to cancer hastened, by the action of a variety of nonspecific irritants. With most nonspecific irritants this facilitation is far less effective than it is with a true carcinogen.

JOHN L. LANDOUST M.D.

EXPERIMENTAL SURGERY

Moyer, C. A., Collier, F. A., Job, V., Vaughan, H. H., and Marty, D.: A Study of the Interrelationship of Salt Solutions, Serum, and Debrinated Blood in the Treatment of Severely Scalded Anesthetized Dogs. *Ann. Surg.* 944, 20, 167.

Saline-bicarbonate solution is more effective than Ringer's-lactate solution, and Ringer's-lactate solution is more effective than "isotonic" sodium-chloride solution in prolonging the life of anesthetized dogs when an amount of these solutions equal to 10 per cent of the animals' body weight is given intravenously before the animals are scalded (two-thirds body surface at 85 C. for thirty seconds). The presence of the bicarbonate ion or the potential bicarbonate ion in the lactate solution appears to be responsible for the superiority of the Ringer's-lactate and the saline-bicarbonate solutions.

The combination of massive transfusions of debrinated blood and oral administration of saline-

bicarbonate solution was the only form of therapy employed that prevented shock without inducing complications that were incompatible with life.

The other forms of therapy employed namely (1) saline-bicarbonate (intravenous), (2) saline bicarbonate (intravenous) and serum (intravenous) (3) serum (intravenous) and saline-bicarbonate by stomach and (4) defibrinated blood (intravenous) and water ad libitum prolonged life and in a number of instances prevented shock. However all of the animals that did not die of shock during the first twenty-four hours died later of complications that seemed to be related to the therapy rather than to the trauma.

A hematocrit of from 80 to 85 per cent does not prohibit the use of transfusions of whole blood.

JOHN J. MALONEY, M.D.

Elman, R.: The Influence of Ether, Morphine and Nembutal on the Mortality in Experimental Burns. *Ann Surg.*, 1944, 110: 211.

Experiments show that the early mortality following severe thermal injury is profoundly influenced by the type of sedation and anesthesia used. A series of experiments were carried out in which severe burn stimulus (immersion up to the axilla at 100 C. for ten seconds) was employed in a series of 10 experiments each. Various doses of morphine in combination with nembutal or ether were used in each group.

Morphine increases the twenty-four hour mortality (up to 100 per cent) in severe experimental burns particularly when given in large doses and with nembutal. Practically no twenty-four hour mortality occurred when ether alone was employed. It is inferred that large doses of morphine when used in the absence of pain may increase the early mortality in severe human burns.

LOUIS T. BYRNE, M.D.

HOSPITALS; MEDICAL EDUCATION AND HISTORY

Adams, J. M.: Stanocola Medical Care Plan. *J Am M Ass* 1944, 126: 333.

The features of the Stanocola Medical and Hospital Association are as follows:

1. It was conceived and organized and is owned, supported and operated by employees.
2. Membership is entirely voluntary.
3. It supplies necessary medical hospital and nursing services to employee members and to their families.
4. There is only one rate of dues regardless of the number of dependents.
5. The medical staff is on salary and mainly on full time.

Although it is owned and operated by the employees the company is much interested in its success and lends its support by

1. Making payroll deduction of the dues.
2. Permitting deduction of the dues from the company thrift fund. This fund is supported by

regular voluntary contributions by employees and by the company. Dues collected from this fund as 85 per cent of them are, represent both employee and company contributions. Through the medium of this fund, members of the association thus receive material help from the company in the payment of their dues.

3. The company has aided the association substantially by making a large donation toward the purchase of its clinic building and on other occasions has made contributions for special purposes.

4. The board of directors of the association has always included two or more of the company's executives elected by the membership. The association is entirely distinct from the company's medical department whose work is limited to industrial medicine—preventive medicine and the care of industrial injuries and diseases.

This plan was put into effect in April 1924 as a result of the reduction of income on the part of the employees of the company who had been unable to secure a reduction in prices and fees to equalize their loss of income. At this time the project was placed on an experimental basis since there were then no Blue Cross hospital plans. The first arrangement was one in which 1,300 employees made an agreement with 4 physicians to pay a retainer of one dollar annually per membership. The physicians divided this fund and agreed to treat the subscribers for one half of the usual fees. This arrangement was unsuccessful and therefore was not renewed after one year.

The Stanocola Medical and Hospital Association was then formed with 2,200 subscribers. In the beginning arrangements were made with private practitioners to treat those eligible in the doctors' own offices. In the panel were a surgeon who served as medical director and an ear, nose and throat specialist. After six months of operation clinic space was rented and all of the physicians except the surgeon and medical director were included on this basis. In 1931 larger quarters were obtained and the staff increased to 11 doctors on full time and 5 on part time. In addition to the medical staff 6 nurses, 2 laboratory technicians, an x-ray technician, 2 office girls, and a cleaning staff were employed and a couple living in the garage answered telephone calls when the offices were closed. The character of the medical staff is excellent, all members being graduates of approved medical schools and most of them having had postgraduate training.

Aid provided starts with medical and surgical services limited only by the capacity of the staff. Patients are treated in the clinic, in the hospitals or in their homes within a radius of seven miles of the clinic, as indicated. Beyond the 7 mile limit a small mileage fee is paid by the patient to the doctor. Hospitalization is at ward rates except that private rooms are provided for contagious diseases and when privacy is a necessary part of the treatment. The general hospitals in Baton Rouge are used and

accord special rates to the association. Special nurses are provided when they are considered necessary. Hospitalization and nursing costs are limited to \$250 for each case.

The average cost to each member of the Association per month is \$3.50.

The advantages to the members are as follows:

1. The members of the association have adequate medical, hospital, and nursing care for themselves and for their families at a predetermined cost. The total cost is probably as great as if the group purchased the service individually, but it has probably received more service than it would have purchased as individuals.

2. The members have been supplied with services at least the equal in quality of that otherwise available and superior to that usually received by persons in the same economic group. They have had the advantage of much freer consultation with specialists than they would have had otherwise, and laboratory and x-ray examinations are more freely used.

3. They have escaped a not infrequent cause for strangling debt—large medical and hospital bills.

4. They have the satisfaction of providing this care for themselves and their families by their own efforts rather than having it handed to them.

The advantages to the employer are as follows:

1. Adequate medical care for the employee is provided with return to duty with the minimum loss of time.

2. Close co-operation exists between the company's medical department and the employee's physician.

3. It is easier to persuade employees to have physical defects corrected than it would be otherwise.

4. Fraudulent claims of industrial injury are reduced.

5. The morale of the employees is improved by freedom from worry over costs of illness and by the satisfaction of providing such excellent medical care through their own efforts.

The advantages to the medical staff of the association are:

1. The compensation is probably higher than the average in the community in normal times.

2. The inconvenience of carrying on an individual business is avoided.

3. Each physician has one day off each week and an annual vacation with pay.

4. Postgraduate training at the expense of the association is provided on occasions.

5. The close association and consultation with other physicians stimulates them to better work.

BENJAMIN GOLDBMAN, M.D.

April, 1945

International Abstract of Surgery

*Supplementary to
Surgery, Gynecology and Obstetrics*

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INTERNATIONAL ABSTRACT OF SURGERY

VOLUME 80

APRIL, 1945

NUMBER 4

ABSTRACTS OF CURRENT LITERATURE SURGERY OF THE HEAD AND NECK

HEAD

Wissenfeld, I. H. and Phillips, E.: Thrombophlebitis of a Cavernous Sinus following the Extraction of Teeth: Cure with Penicillin and Heparin. *Arch. Otolar., Chic.* 1944 40 497

Prior to the day of sulfonamide therapy recovery from thrombophlebitis of a cavernous sinus was extremely rare. With the advent of these compounds reports of cures began to appear following the administration of sulfanilamide, sulfapyridine, sulfathiazole, and presumably, sulfadiazine. The use of anticoagulants, especially heparin as adjuvant therapy seemed to enhance the value of the sulfonamide compounds but this was by no means proved. Recovery from cavernous-sinus thrombophlebitis with penicillin therapy has been reported.

The case reported by the authors illustrates again the danger of performing an operation on the maxilla and the palate in the presence of acute sinusitis. Thrombophlebitis of a cavernous sinus developed in the presence of an adequate sulfadiazine level in the blood. A dramatic recovery followed the administration of penicillin and heparin.

NOAH D. FABRICANT M.D.

EYE

Pfeiffer, R. L.: Localization of Intraocular Foreign Bodies by Means of the Contact Lens. *Arch. Ophth., Chic.*, 1944, 33 261

The author discusses the roentgenological localization of intraocular foreign bodies with the aid of a contact lens. The lens which is made of plastic material, is of average scleral radius (21 mm.) and corneal radius (8 mm.).

In Vogt's method of taking bone-free roentgenograms for localizing fragments in the anterior 8 to 12 mm. of the eye an ordinary dental film is held over and perpendicular to the inner canthus and the rays are directed from the side so that a shadow of the profile of the anterior segment of the eye is recorded.

The method which utilizes the contact lens with radiopaque markers is recommended as most ac-

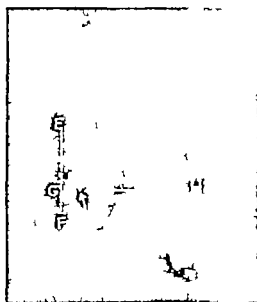


Fig. 1. Lateral view of an intraocular foreign body with a line drawn anterior to the markers to indicate the plane of the limbus (EF). GH is drawn at right angles to EF and through the foreign body indicated by an arrow.

curate. It requires 2 roentgenograms, a postero-anterior and a lateral.

After these are taken lines are drawn on the films to indicate the relationship of the foreign particle to the contact lens, and the location is then shown on charts that represent an anteroposterior view of the eye and a cross-section cut in the meridian in which the foreign body lies. The position of the foreign body is plotted by drawing a horizontal line on the x-ray film across the orbits several millimeters below the upper margins, then drawing a horizontal and vertical line through the shadows of the markers on the contact lens to locate the center of the lens. A line is then drawn to bisect the foreign body and pass through the center of the lens. The angle formed by this line with the horizontal line through the upper part of the orbit is measured with a protractor and a corresponding line at this

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intramuscular injections of 150 units in 2 cc. of saline solution every three hours for a period of forty-eight hours. Experimental work indicates that this probably gives a concentration of penicillin in the tissues that is too low to be effective, and that probably much larger doses must be used if they are to be of any value. This is borne out by the clinical results, which have been most disappointing in the treatment of posterior uveal infections.

The results obtained in the treatment of infections of the anterior segment of the eye by topical instillation of penicillin are much more encouraging. Aqueous solutions require very frequent use and an ointment would appear to be the most satisfactory. Four ointments were tested for their penetrability: simple ointment, oil-in-water, emulsion, and lubricating jelly. They were found effective in the order named. Penicillin showed the greatest penetrating power when placed in a "vanishing" stearate type of base and while this may be used on the skin of the lids, its use on the conjunctival sac is not advised because of possible damage to the corneal epithelium. The simple ointment found best for conjunctival use was made by adding 25,000 units of penicillin dissolved in 0.25 cc. of distilled water to 10 gm. of simple ointment (U.S.P.). It is advisable to make up no more than is required for a twenty-four to forty-eight hour period and to keep the ointment on ice, because the substance usually deteriorates at a rapid rate.

Penicillin used locally was found effective in the clinical treatment of acute and chronic infections of the lids, conjunctiva, and cornea which had been produced by penicillin sensitive organisms. In 10 of 12 cases of acute staphylococcal conjunctivitis the condition was cured within forty-eight hours. Cases of chronic conjunctivitis which had resisted ordinary methods of treatment for months or years were usually arrested within a week. In the acute cases hourly applications of penicillin day and night, are most effective. In the chronic cases it should be applied during the waking hours only.

It is pointed out that susceptible individuals may become hypersensitive to penicillin. This heretofore unreported occurrence was noted in 4 of the 46 patients who received treatment.

WILLIAM A. MANN, M.D.

RAR

Benham, T. M.: The Conservative Treatment of Chronic Suppurative Otitis Media in Adults. *J. Laryngol.*, Lond. 1944 59 117

Cases of chronic suppurative otitis media constitute a large part of the cases coming to the outpatient department at ear, nose and throat centers of the R.A.F. The results of treatment of 200 consecutive unselected cases are presented.

The method of treatment was based on the thesis that thorough cleaning of the ear was most essential. For best results endaural manipulations should be carried out personally. Aural polypi and granula-

tions were removed. Flat granulations were cauterized with trichloroacetic acid and the middle ear was emptied by suction through a cannula by means of eustachian inflation, after which dry powder was insufflated. Sulfathiazole powder seemed preferable to boric powder with 1 per cent iodine. A gauze wick soaked with antiseptic solution was left in the meatus.

The treatments varied from twice a day to once a week, the wick being removed after forty-eight hours or when soaked.

Eighty-two and one-half per cent of the ears became dry. 8 1/2 per cent became quiescent, and the remainder were unaffected. Those with central perforations became dry in over 90 per cent of the cases; those with attic perforations became dry in 83 per cent, and with marginal perforations in 49 per cent. Central perforations not involving the fibrocartilaginous ring surrounding the pars tensa were found in over 66 per cent of the cases and these responded best to conservative treatment. The attic perforations usually had localized disease in the anterior or posterior pouch of Troeltsch or in Prussak's pouch. When the perforation was large the prognosis was good, but extensive cholesteatoma could not be cured without surgery. Marginal perforations respond poorly because of bone necrosis. Polypi or granulations arising from the tympanic cavity were evidence of diseased bone and usually required surgery. The majority of the ears in the successful cases became dry in less than one month. Ears which had not become dry after two months of continuous and thorough treatment usually required surgery.

JOHN R. LINDSAY, M.D.

Hall, I. S.: The Surgical Treatment of Otosclerosis. *Proc. R. Soc. M.*, Lond. 1944, 37 737

The main object of surgery for otosclerosis has been to replace the immobilized stapes by a movable membrane, but whether this is justified is still open to question.

The author has experimented with placing the fenestra first over the canal, but he has placed it over the ampulla in all his latest cases.

Local anesthesia is used to the stage of opening the labyrinth when pentothal sodium is given intravenously as long as necessary.

The results of 66 operations are difficult to evaluate since various techniques were used, but it was found that if improvement is maintained for four months after the operation it is likely to persist for some time.

There have been very few complications and these were of a minor nature. No cases of facial paralysis or labyrinthitis were reported.

The selection of patients influences the results greatly; the younger seem to do better. Reliance is placed on the use of the monochord for determining bone conduction in the higher frequencies. Lack of appreciation of the upper tones by bone conduction has proved to be a contraindication to operation.

JOHN F. DIXON, M.D.

angle is plotted on a chart representing the front view of the eye. Then the distance of the foreign particle from the center of the contact glass is measured with a compass and millimeter rule. This measurement (minus a correction for the magnification of the lens) is transferred to the chart. It represents the distance of the foreign body from the anteroposterior axis of the eyeball. The correction factor depends on several variables.

On the film of the lateral view (Fig. 1) a line (EF) is drawn across the shadow of the contact lens anterior and tangential to the markers of the lens so that the limbus is located. Another line (GH) is drawn perpendicular to the first through the foreign body and the distance along the line from the foreign body to the plane of the limbus is measured. This measurement (corrected for magnification) represents the actual distance of the foreign body behind the plane of the limbus.

The location of the foreign body is plotted on a chart which represents a front view and also a section of the eyeball. To increase the accuracy in plotting, the charts are made three times the normal size of the eye. Before making the incision for removal of the foreign body the surgeon should use a Gohst protractor to mark the exact meridian in which the foreign body lies, utilizing peripheral scratches on the cornea stained with fluorescein.

JOSHUA ZUCKERMAN, M.D.

Smolzer, G. K., and Ozanian, V.: Chemotherapy and Corneal Burns. *Am. J. Ophth.*, 1944, 37, 1003.

The purpose of this study was to determine which of the chemotherapeutic agents applied locally to the cornea interfered least with the reproduction of healthy epithelial cells or with the migration of these cells over a denuded area following an injury. This was carried out by counting the cells in mitosis in control eyes and in those treated with the sulfonamides and penicillin. Standard burns or abrasions were produced in one eye of rats the opposite eye being used as a control. Abrasions were produced in the form of a 1 mm. band of removed epithelium from limbus to limbus. Burns were made with the Shaban thermophore at a constant temperature and applied for a constant duration of time. The sulfonamides were applied as fine powders or as a 5 per cent ointment in a lanolin base.

Most of the sulfonamides had no deleterious effect on the cell-division rate in the intact cornea no matter in what form they were applied. Penicillin, likewise, showed no effect in these cases. It was concluded that the corneal abrasions healed without a marked increase in the number of mitotic figures. Thermal burns became covered in about the same length of time as did abrasions (from twelve to eighteen hours) but a great increase in the number of mitotic figures occurred in the process. Sulfacetamide, sulfapyridine, and penicillin had no effect on cell division in the intact rat cornea. Sulfadiazine seemed to increase cell division, and sulfathiazole to depress mitosis.

In general, the chemotherapeutic agents tested had no unfavorable effect on the abraded cornea and did not interfere with cell division in burned corneal epithelium. Sulfathiazole and sulfacetamide inhibited cell migration following corneal burns, whereas sulfadiazine and penicillin were but slightly detrimental. The sulfonamides used in the form of ointments inhibited cell migration slightly less than those used in powder form.

WILLIAM A. MANN, M.D.

Kayes, J. E. L.: Penicillin in Ophthalmology. *J. Am. M. Ass.*, 1944, 126, 610.

The contents of this article were gathered at the special penicillin research center at Bushnell General Hospital, Brigham City, Utah, from private communications of medical officers of the Army and from medical literature on penicillin. The research was carried on to determine the usefulness of the drug in ophthalmology.

As a result of the appraisal of penicillin, a study of the illustrative cases treated, the research on medication and dosage, and the notations of complications following its use, the following are some of the comments the author has made:

1. Penicillin is the drug of choice in the treatment of ophthalmic diseases secondary to infection with gonococci, streptococci, and sensitive staphylococci; it should be tried also in diseases caused by bacteria meningitidis, micrococcus catarrhalis, and pneumococci.

2. Penicillin, when effective, affords relief, usually promptly and sometimes startlingly. This relief is often better than that from other types of treatment.

3. Penicillin can be saved in considerable amounts by identifying the bacteria before treatment is instituted.

4. Penicillin is recommended as a prophylactic in certain intraocular operations and ocular injuries.

5. Penicillin given early and in large doses, is indicated in orbital cellulitis secondary to paranasal sinus infection and infection involving the venous dural sinuses.

6. Penicillin solutions because of their instability do not lend themselves to office and home medication as readily as more stable drugs. Penicillin ointment is reasonably stable for at least a month at room temperature and for six months in a commercial refrigerator.

7. Penicillin is destroyed by heat; therefore sterilization is not feasible.

LEONARD L. MCCOY, M.D.

Ballows, J. G.: Penicillin Therapy in Ocular Infections. *Am. J. Ophth.*, 1944, 37, 205.

Only by the injection of large amounts of penicillin intramuscularly or intravenously can a measurable amount of penicillin be found in the posterior portion of the globe of the eye. In cases of infections involving this portion of the eye, it has been recommended that 100,000 units be administered intravenously over a seventeen hour period, followed by

intramuscular injections of 1250 units in 2 cc. of saline solution every three hours for a period of forty-eight hours. Experimental work indicates that this probably gives a concentration of penicillin in the tissues that is too low to be effective, and that probably much larger doses must be used if they are to be of any value. This is borne out by the clinical results, which have been most disappointing in the treatment of posterior uveal infections.

The results obtained in the treatment of infections of the anterior segment of the eye by topical instillation of penicillin are much more encouraging. Aqueous solutions require very frequent use and an ointment would appear to be the most satisfactory. Four ointments were tested for their penetrability: simple ointment, oil in water, emulsion, and lubricating jelly. They were found effective in the order named. Penicillin showed the greatest penetrating power when placed in a vanishing stearate type of base, and while this may be used on the skin of the lids, its use on the conjunctival sac is not advised because of possible damage to the corneal epithelium. The simple ointment found best for conjunctival use was made by adding 25,000 units of penicillin dissolved in 0.25 cc. of distilled water to 10 gm. of simple ointment (U.S.P.). It is advisable to make up no more than is required for a twenty-four to forty-eight hour period and to keep the ointment on ice, because the substance usually deteriorates at a rapid rate.

Penicillin used locally was found effective in the clinical treatment of acute and chronic infections of the lids, conjunctiva, and cornea which had been produced by penicillin-sensitive organisms. In 10 of 12 cases of acute staphylococcal conjunctivitis the condition was cured within forty-eight hours. Cases of chronic conjunctivitis which had resisted ordinary methods of treatment for months or years were usually arrested within a week. In the acute cases hourly applications of penicillin day and night are most effective; in the chronic cases it should be applied during the waking hours only.

It is pointed out that susceptible individuals may become hypersensitive to penicillin. This heretofore unreported occurrence was noted in 4 of the 46 patients who received treatment.

WILLIAM A. MANN, M.D.

RAR

Banham, T. M.: The Conservative Treatment of Chronic Suppurative Otitis Media in Adults. *J. Laryngol.* Lond. 1944, 59, 117

Cases of chronic suppurative otitis media constitute a large part of the cases coming to the out-patient department at ear, nose, and throat centers of the R.A.F. The results of treatment of 300 consecutive unselected cases are presented.

The method of treatment was based on the thesis that thorough cleaning of the ear was most essential. For best results endaural manipulations should be carried out personally. Aural polypi and granula-

tions were removed; flat granulations were cauterized with trichloroacetic acid; and the middle ear was emptied by suction through a cannula by means of eustachian inflation after which dry powder was insufflated. Sulfathiazole powder seemed preferable to boric powder with 1 per cent iodine. A gauze wick soaked with antiseptic solution was left in the meatus.

The treatments varied from twice a day to once a week, the wick being removed after forty-eight hours or when soaked.

Eighty-two and one-half per cent of the ears became dry; 83½ per cent became quiescent, and the remainder were unaffected. Those with central perforations became dry in over 90 per cent of the cases; those with attic perforations became dry in 83 per cent, and with marginal perforations in 40 per cent. Central perforations not involving the fibrocartilaginous ring surrounding the pars tensa were found in over 66 per cent of the cases and these responded best to conservative treatment. The attic perforations usually had localized disease in the anterior or posterior pouch of Troeltsch or in Prussak's pouch. When the perforation was large the prognosis was good, but extensive cholesteatoma could not be cured without surgery. Marginal perforations respond poorly because of bone necrosis. Polypi or granulations arising from the tympanic cavity were evidence of diseased bone and usually required surgery. The majority of the ears in the successful cases became dry in less than one month. Ears which had not become dry after two months of continuous and thorough treatment usually required surgery.

JOHN R. LINDSAY, M.D.

Hall, I. S.: The Surgical Treatment of Otosclerosis. *Proc. R. Soc. M., Lond.* 1944, 37, 757

The main object of surgery for otosclerosis has been to replace the immobilized stapes by a movable membrane, but whether this is justified is still open to question.

The author has experimented with placing the fenestra first over the canal, but he has placed it over the ampulla in all his latest cases.

Local anesthesia is used to the stage of opening the labyrinth when pentothal sodium is given intravenously as long as necessary.

The results of 66 operations are difficult to evaluate since various techniques were used, but it was found that if improvement is maintained for four months after the operation it is likely to persist for some time.

There have been very few complications and these were of a minor nature. No cases of facial paralysis or labyrinthitis were reported.

The selection of patients influences the results greatly; the younger seem to do better. Reliance is placed on the use of the monochord for determining bone conduction in the higher frequencies. Lack of appreciation of the upper tones by bone conduction has proved to be a contraindication to operation.

JOHN F. DEXTER, M.D.

NOSE AND SINUSES

Seltzer A. P.: The Nasal Septum; Plastic Repair of the Deviated Septum Associated with a Deflected Tip. *Arch. Otolaryng. Chic.* 1944, 40: 433.

The author reviews the embryonic development anatomy and physiology of the nose, and discusses the pathology of the nasal septum. He describes the surgical method necessary for correction of the deflected cartilaginous tip of the nose associated with a deviated septum and gives the technique in detail. The method consists essentially in the uncovering of the nasal framework before correction of the septal deformity is attempted. The skin over the bony and cartilaginous bridge, along with the tip, alae, and columella are thereby freed from the septal cartilage, the upper lateral cartilages, and nasal bones. When the septal cartilage has been brought back to the midline position and sutured to the columella the deformity of the nasal tip is corrected. The septum deformity is corrected by incision on the convex side and subperichondral removal of a narrow vertical strip of cartilage from the dorsum to the base followed by incision through the cartilage along its base. This allows the septal cartilage to straighten when sutures are used to approximate the wound edges. JOHN R. LINDSAY M.D.

MOUTH

MacGregor A. B., and Long, D. A.: Penicillin Pastilles for Oral Infections. *Brit. M. J.* 1944, 2: 686.

Penicillin contained in pastilles was used in the treatment of several types of oral infections. Each pastille contained 500 units of penicillin and its content in the saliva was estimated after periods of fifteen and thirty minutes. These studies showed the penicillin to be present in large quantities up to fifteen minutes after the pastille had melted in the mouth. The penicillin pastilles retained their potency three months after their preparation. Bacteriological studies revealed that it was possible to reduce greatly the number of bacteria in the mouth, and even to produce sterile cultures. Patients with ulcerative gingivostomatitis, acute streptococcal tonsillitis, and other types of postoperative dental infections were treated, as well as chronic streptococcal carriers.

The clinical and bacteriological effect of penicillin pastilles in 25 cases of Vincent's disease was noted. All of the patients became asymptomatic in twenty-four hours, with disappearance of the characteristic fetor. In forty-eight hours, the slough disappeared and all signs of inflammation were gone. Bacteriological studies showed rapid disappearance of the spirochaetes and the fusiform bacilli. After seventy-two hours, films showed a preponderance of epithelial tissue and few organisms.

Seventeen patients with acute tonsillitis, pyrexia, and the demonstrable presence of Lancefield group A hemolytic streptococcus were treated. In forty

eight hours, local and general symptoms were completely relieved. The bacteriological course paralleled the clinical course. Controls treated with serum and sulfonamides failed to show such striking improvement. The majority of chronic streptococcal throat carriers treated with penicillin pastilles gave negative cultures within seventy-two hours of treatment. However throat cultures became positive within six days after cessation of the penicillin applications. Three compound fractures of the jaw previously showing marked evidences of oral sepsis responded so rapidly to the penicillin pastilles that within twenty-four hours fixation and splinting of the mandible became possible. Severe ulcerations of the mouth associated with pneumococcal and hemolytic streptococcal infections healed rapidly and no organisms were demonstrable after twenty-four hours of treatment. Patients from whom the micrococcus catarrhalis, haemophilus influenzae, and hemolytic streptococcus were obtained from the tonsillar beds after tonsillectomy also responded well to the oral penicillin treatment.

BENJAMIN G. P. SCHAFFROFF M.D.

NECK

Vasconcelos, E., and Barretto, P. De M.: Total Laryngectomy; Simplified Techniques with the Use of a Special Clamp Which Makes Possible the Removal of the Larynx and Pre-Epiglottic Space without Opening of the Pharynx. *Arch. Otolaryng. Chic.*, 1944, 40: 375.

A technique is described for a conservative total laryngectomy in which a special clamp is used this clamp permits removal of the larynx and pre-epiglottic space in a single block and makes the suture of the larynx simple and safe. In the preparation of the patient, morphine, scopolamine, and sparteine sulfate are given subcutaneously forty-five

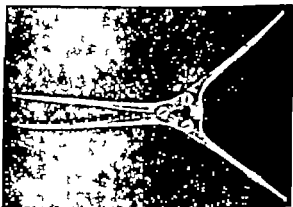


Fig. 1. The original Vasconcelos clamp, especially devised for suture of the pharynx. Barretto modification of the Vasconcelos clamp consists in having teeth in both blades of the clamp instead of in only one blade. This aids greatly in preventing the escape of the pharyngeal mucus when the larynx is removed.

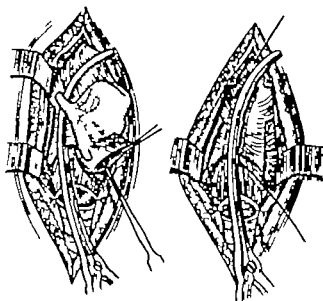


Fig. 2. Eighth step in the conservative technique removal of the larynx and suture of the pharynx.

minutes before operation. Anesthesia is induced one half hour later by a solution of tribromethanol in amylen hydrate (from 0.08 to 0.10 gm. per kilogram of body weight). Intratracheal insufflation of ether may be added.

The simple laryngectomy operation is done in a narrow field through a midline incision making an exposure from the hyoid bone down to the thyroid isthmus. The hyoid is sectioned and the mylohyoid muscles are separated for a distance of 1 cm. The trachea or cricoid ring is sectioned and the larynx dissected free from below upwards. The dissection of the posterior surface of the cricoid is carried up to the transverse fibers of the arytenoid transversus muscle, the pharyngeal wall is separated from the posterior surface of the thyroid cartilage and the superior cornua are cut across. By means of a hook passed up through the larynx the epiglottis is pulled downward so as not to be caught in the clamp which is then put in place to cut off the larynx and pre-epiglottic space from the pharynx. After removal of the larynx by incision along the concave border of the clamp, a continuous suture is temporarily passed beneath the clamp and held by the two ends while the clamp is removed then a continuous suture of chromic catgut No. 000 or 0000 is placed in the Cushing manner and reinforced by interrupted sutures. The temporary suture is then removed.

A second technique is described for cases in which the prelaryngeal muscles and hyoid bone are to be removed. A transverse incision is used at the upper

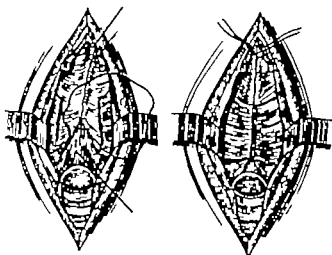


Fig. 3. Left, Placing of the second sutures in the Cushing manner (Eighth step). Right, Ninth step in the conservative technique approximation of the constrictor muscles of the pharynx.

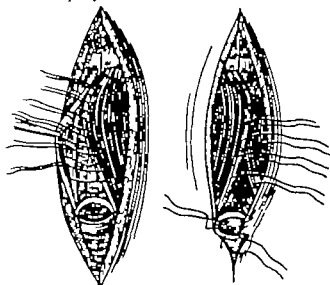


Fig. 4. Use of the Crowe and Broyles technique in the overlapping of the prelaryngeal muscles (ninth step).

third of the thyroid cartilage. The tracheal stump is later brought through a circular opening in the lower flap.

In this operation the hyoid bone is dissected free. All muscles attached to its superior border are cut with the electric knife the bone then being removed with the prelaryngeal muscles and larynx. The clamp is placed in position in a way similar to the former method the larynx cut free along its border and the pharynx closed as in the simple operation.

JOHN R. LEMBRAY, M.D.

SURGERY OF THE NERVOUS SYSTEM

PERIPHERAL NERVES

Larje, A., and Heinbecker, P : Nerve Degeneration Following Prolonged Cooling of an Extremity
Ann. Surg. 1944, 120 742.

The effects of prolonged immersion cooling have not been fully verified by experimentation. Twenty dogs were used for this study. The animals were placed in a hammock with one forelimb immersed in cold water for ninety-six hours. A temperature of 6°C. was maintained constantly during this time. The animals were then sacrificed at intervals up to three months.

Immediately after the immersion the limb was swollen and showed either complete or partial loss of sensation and motor power. The threshold of faradic stimulation increased until about the fifth day when a response could no longer be obtained. It gradually returned to normal by the sixteenth day.

The generalized edema in the earlier period persisted longer in the nerves—at least ten days. After the edema had subsided, histological study revealed that in addition to a questionable fibrosis of the cutaneous and subcutaneous tissues there was a marked degeneration of all the peripheral nerves.

The extensive nerve damage in the early stages without signs of inflammation or damage to the other tissues suggests that later degenerative changes in the other tissues are secondary to neural destruction and ischemia. Unless amputation of the area is to be performed, therapeutic refrigeration should be used only with consideration of the possible late effects.
JACK WOOLR M.D.

Davis, L., Hillier F. Perret, G. and Carroll, W.
The Effect of Sulfonamides upon Experimental Gunshot Wounds Involving the Peripheral Nerves. *Ann. Surg.* 1944, 20 494.

War wounds are usually associated with rather extensive destruction of the tissues, as well as with fractures, and are contaminated or grossly infected. The liberal use of sulfonamide drugs, with débridement, is to be considered in an effort to control the course of the infection. In view of this, it was believed that the effect of sulfonamides upon the repair and regeneration of peripheral nerves should be determined. If the use of sulfonamide drugs would hasten recovery from infection, and therefore allow peripheral nerve repair at an earlier date—with no deleterious effect upon nerve regeneration—the ultimate functional result would be improved.

An experimental study was undertaken, in which gunshot wounds were produced in the sciatic nerve of cats. Débridement of the wound and simultaneous repair of the nerve were performed immediately and at various intervals, until forty-eight hours after the injuries. The gross appearance of the wounds treated surgically six hours after injury was indis-

tinguishable from that of wounds treated immediately after injury except for an occasional edema. Wounds which remained untreated for more than twelve hours showed characteristic signs of infection. Various sulfonamide drugs, including crystalline sulfanilamide, powdered sulfathiazole, and sulfadiazine, were introduced locally into the wound at the time of débridement.

In spite of careful débridement performed immediately after the injury the rate of infection and of formation of extensive abscesses was very high when the sulfonamides were not used in the wounds locally. The rate of massive infection increased, the longer débridement was delayed. Massive infection resulted in 38.2 per cent of the animals treated immediately after injury and in 31.9 per cent of the animals operated upon six hours after injury. The percentages of infection rose further the longer the interval became between injury and surgical repair.

In the animals treated locally with sulfonamides, infection developed in 5 per cent of those which had been treated immediately and in 10 per cent of those débrided after six hours and in 26 per cent and 55.5 per cent, respectively of the groups treated from twelve to eighteen hours, and from eighteen to twenty four hours after the injury.

It was believed that in some instances adhesions were firmer in those cases in which sulfanilamide had been used locally in the wound, in contrast to those cases in which it had not been used.

A further experiment was conducted by sectioning the sciatic nerve in cats, with aseptic conditions in one group and septic conditions in another. The developing infections were treated with the various sulfonamides and in some instances the nerve was merely exposed, the drug applied upon it, and the wounds observed at intervals thereafter.

The wounds treated with sulfonamide compounds were characterized by an increased amount of adhesions fixing the nerve to the surrounding tissues. This was a constant finding in those cases which had been sectioned and sutured, or in which a graft had been used to effect a repair and these adhesions occurred whether or not the operation had been performed with aseptic or septic technique.

A study of the points of suture revealed no conclusive evidence that the regeneration of nerve fibers, axon-cylinder formation, myelination, or the absorption of myelin decomposition products was changed by the use of the sulfonamide drugs.

HOWARD A. BROWN, M.D.

Tarlov I. M : Autologous Plasma Clot Suture of Nerves; Its Use in Clinical Surgery *J. Am. M. Ass.* 1944, 26 741.

Although nerve suture has been relatively satisfactory, it has some shortcomings. It is difficult to avoid the inclusion of nerve fibers in the sutures to

avoid knuckling of the fibers when the knots are tied, and to avoid axial rotation of the nerves at times when the sutures are inserted. Recently a fine tantalum wire has been used and although there is less fibrotic reaction, there are the same objections to the wire as to silk sutures. Recent experiments with fortified cockerel plasma clotted with chick embryo extract for approximating the nerve ends has given very good results. However, there was an appreciable inflammatory and fibrotic reaction in connection with this procedure.

The author studied the various tension strengths of various plasma compounds and chose to use autologous unmodified plasma around which there was very little inflammatory or fibrotic change. Certain difficulties were found in holding the ends of the nerve together during the application of the plasma, and after a long series of experiments a rubber mold was devised for this purpose. The use of the mold with the unmodified autologous plasma in the suture of peripheral nerves led to satisfactory functional recovery. Fourteen cases so treated are reported and in about half of these sufficient time has elapsed to draw satisfactory conclusions. Some of the cases were checked by chromaxia studies. From 2 to 3 fine tantalum-wire tension sutures were considered to be a further advantage when plasma was used for nerve suture. Clinical results are satisfactory and further work with this method should be encouraged.

ADRIEN VERHUGGHEM M.D.

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Wood, E. H., Jr.: Some Roentgenological and Pathological Aspects of Calcification of the Choroid Plexus. *Am. J. Roent.* 1944, 52: 358.

Calcified bodies seen in the x rays of the skull are likely to lead to some confusion unless they can be identified as normal structures. The pineal body is frequently seen in the midline. Occasionally however parts of the choroid plexus are calcified, especially at the glomus which is situated at the atrium of each lateral ventricle. The calcification thus seen is usually fairly symmetrical though it may vary in density on the two sides. The calcification is due to regressive changes in the choroid plexuses. These changes are quite common.

On examination of the calcified areas it was found that they were composed of psammoma bodies in the connective tissue of the plexus. These bodies are common in all the membranes of the brain and spinal cord, but when gathered together in the plexus they constitute bilateral areas of calcification. The areas have been described as similar to popped kernels of corn or a collection of tiny glass beads.

This plexus calcification has been found in children, and 2 examples are mentioned one in a child two and one half years of age and the other in a child three years of age. Both children were very abnormal mentally had convulsive seizures and were diagnosed as having forms of cerebral aplasia.

A case is reported also of calcification in the plexus of the fourth ventricle. This was probably a coincidental finding. Calcification in the plexus may be of clinical significance when displacement of it occurs which would indicate an expanding lesion. Most of the tumors suspected because of displacement of the choroid glomus have been posterior to it, usually in the temporal lobe or in the occipital lobe. Two examples are reported in this article.

The article is written by the successor of Cornelius Dyke who contributed so much to the interpretation of x ray films of the skull in the Department of Radiology of the Neurosurgical Institute of New York.

ADRIEN VERHUGGHEM M.D.

Horwitz, A., and Perroni, J.: Meningococcal Meningitis in Santiago Chile from 1941 to 1943; An Epidemic of 4,464 Cases. *Arch. Int. M.* 1944 74: 365

During an epidemic of meningococcal meningitis that occurred at Santiago Chile, in the years from 1941 to 1943 4,464 persons, or 1 of every 300 inhabitants acquired the disease. The authors have made a study of this epidemic from the viewpoint of mortality morbidity and treatment.

The mortality rate on patients was 16.5 per cent among adults and 28 per cent among infants under four years of age. The authors find fault with the words "epidemic cerebrospinal meningitis," and have adopted the designation of "meningococcal infection." The complications were not numerous because of the use of adequate chemotherapy. There were ocular complications in 5 per cent of the patients, and partial or total unilateral or bilateral deafness in 5 per cent. Other complications referable to the central nervous system were also seen. Arthritis involving one or more joints and varying from the simple painful joint to purulent arthritis, was observed in 10 per cent of the cases. Occasionally the arthritic involvement occurred late in the disease and the sulfonamide drugs apparently had little influence on it. Spinal puncture was performed for diagnostic purposes only. All strains of meningococci isolated from the patients corresponded to group 1 of Griffiths. Group 2 strains were isolated from carriers. Positive blood cultures were obtained in 9.7 per cent of the cases, and positive bone marrow cultures in 14.8 per cent. Chemotherapy was instituted early in the disease. The intrathecal route was not employed. If patients were rational, the oral route was preferred and gavage was used occasionally. For technical reasons blood levels were not obtained and, in any case, it was believed that the general condition of the patient was more important than the blood level.

The authors report the results of their studies on 450 patients divided into three groups of 150 each, which were treated with sulfadiazine, sulfanilamide and sulfathiazole respectively. Eliminating the patients who died within the first twenty four hours, the fatality rates were reduced to 10.7 per cent for the group treated with sulfanilamide, to 6 per cent

for the group treated with sulfathiazole and to 5 per cent for those treated with sulfadiazine.

With regard to the effect of therapy with these drugs, toxic manifestations were observed in 50 of the patients treated with sulfanilamide in 13 of those treated with sulfathiazole and in only 7 of those treated with sulfadiazine.

In conclusion, the authors state that at the present stage of our knowledge sulfadiazine appears to be the drug that is most satisfactory for the treatment of meningococcal infection.

ADRIEN VERBROECKEN, M.D.

SPINAL CORD AND ITS COVERINGS

Woods, W. W., and Piments, A. M.: Intramedullary Lesions of the Spinal Cord; a Study of 68 Consecutive Cases. *Arch. New Psychiat. Chic.*, 1944, 5: 383.

This is an analysis of 68 consecutive cases of intramedullary lesions of the spinal cord, in which operation was performed at the University Hospital, Ann Arbor, Michigan, between 1935 and 1943. In 4 cases the clinical diagnosis was not confirmed by operation, so that really 64 cases were confirmed and 35 of these presented intramedullary tumors. In 4 cases the histopathology was not obtained, in 5 cases there was a hemangiomatous tumor and in 20 cases syringomyelia was present. The symptoms were of relatively long duration in view of the location of the tumor. In 6 cases the symptoms were of ten years duration—they presented 2 ependymomas, mixed glioma, 2 dermoid cysts, and 1 spongioblastoma polare. These 6 cases produced widening of the neural canal in the roentgen pictures. Studies of the spinal fluid revealed block partial or complete in 25 cases. There was no significant correlation between the pathological type of tumor and the presence of

spinal-fluid block or of xanthochromia. There was not any special syndrome which differentiated intramedullary from extramedullary tumor although this statement is somewhat in contradiction to the usually accepted theory.

There are two points with regard to the treatment that the authors emphasize: (1) there should be a vertical chordotomy of the entire length of the tumor just to one side or other of the midline and (2) the dura should be left widely open for the purposes of decompression. In fact, they advocate transverse cuts in the dura as well as the longitudinal incisions. The authors have also compared their own series to those cases that they have found adequately described in the literature, and they are unable to be as optimistic, on the basis of their statistics, as the reports in the literature, especially with regard to complete operative removal of the tumor.

The tumors were classified histologically according to the method of Cushing and Bailey and the modification of Kernohan and various types of gliomas were found with the ependymoma predominance. Melanoblastoma, intramedullary blood clot, and dermoid cysts were also found. Roentgen-ray therapy appeared to be of most value in the ependymomas.

With regard to the patients with syringomyelia, the shortest duration of symptoms was ten days and the longest twenty-one years. The clinical examination confirmed the classical description of the disease. Treatment consisted of operation with vertical incision of the syringomyelic cavity. However, the ultimate results of treatment of syringomyelia have not been nearly as good in the authors' series of cases as the rest of the literature would suggest. There is an extensive bibliography and adequate statistical tables to confirm the points brought out.

ADRIEN VERBROECKEN, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Webster G V: Gynecomastia in the Navy *Md Surg*, 1944, 95 375

In 1942 there was an incidence of 6.96 cases of gynecomastia in the Navy per 100,000 admissions.

The three most commonly ascribed causes of gynecomastia are (1) heredity (2) mechanical stimulation, and (3) hormonal imbalance. The author believes that only the latter two are responsible.

With hypertrophy of the breast in the male there is hyperplasia of periductile connective tissue and an increase of the epithelial lining of the ducts. These ducts may be dilated and even cystlike. Not infrequently, small adenomatous areas surrounded by dense fibrous tissue are present. The microscopic picture is indistinguishable from a fibroadenoma or chronic cystic mastitis in the female.

Treatment of the breast is indicated for cosmetic reasons, and for pain or disability resulting from the size of the enlargement. Endocrine therapy has at best produced only temporary regression.

The author preserves the nipple for psychic reasons. The breast tissue is removed through a tiny circumareolar incision in the lower half of the areolar circumference. Very large masses of breast tissue can be removed through such an incision if the specimen is removed in quadrants or sixths one piece at a time. Care must be taken that no breast tissue is allowed to remain. Hemostasis is secured by pressure and if necessary by suture ligation. Pressure dressings with an abundance of fluffed gauze are applied to prevent postoperative edema and hemorrhage.

EARL O LATIMER, M.D.

TRACHEA, LUNGS, AND PLEURA

Weems, H. S.: Pulmonary Disease Associated with Megacosophagus. *Am. J. Roentg* 1944, 52 472

During the past four years the author has encountered 15 cases of megacosophagus in the Grady Hospital of Atlanta, Georgia. In 5 of these pulmonary complications were demonstrated roentgenologically. Although this incidence may be too high, judging from such a small series of cases, nevertheless it is the author's impression that pulmonary lesions occur in megacosophagus more often than is generally appreciated. The complications in the 5 cases, which are individually reported, represented pulmonary abscess, aspiration pneumonia (in 3 cases), pulmonary fibrosis and bronchiectasis.

The interesting feature is that in 3 of the 5 cases the respiratory symptoms had completely overshadowed the digestive disturbances so that the presence of the megacosophagus was almost missed. In 2 cases the symptoms of esophageal disease were established only after re-investigation. The third case, even after the condition was recognized would

not admit symptoms which would make the examiner suspect esophageal disease. For this reason it is important that during the cursory roentgen examination of the chest in such cases, certain signs be found which direct the attention to the possible involvement of the esophagus so that a supplemental contrast medium study of the latter is undertaken. The author enumerates several roentgenographic and roentgenoscopic findings as of very definite help. The enlarged esophagus produces a widening of the mediastinal shadow toward the right side extending from the base of the neck to the diaphragm. The shadow of the esophagus may simulate the right border of the heart which gives the impression of an enlargement of the right side of the heart. Tendency toward pouch formation may result in a scalloped or lobulated sometimes bizarre appearance of the mediastinal shadow. In the presence of numerous small gas bubbles the mediastinal shadow may appear mottled and occasionally there is a fluid level. In the lateral view a forward displacement of the trachea may be noted. The most helpful sign, however, is the demonstration of a double air column overlying the upper dorsal spine in the posteroanterior view. The central air column represents the trachea which is seen through the air column of the upper dilated esophagus.

Whenever any of these findings is present a subsequent contrast medium examination of the esophagus will permit the establishment of the diagnosis of megacosophagus or a differentiation from mediastinal disease and lesions of the spinal column without difficulty.

It is the author's opinion that the pulmonary complications in megacosophagus are the result of aspiration into the bronchial tree of food particles regurgitated from the esophagus into the pharynx as is so often noted in this condition. Pulmonary fibrosis is believed to form a sequela of recurrent aspiration pneumonia, especially since several investigators reported in the literature the isolation from the sputum of such patients of a nonpathogenic, acid fast micro-organism which is identical to that isolated from various fruits and vegetables. If one accepts the occurrence of a pulmonary fibrosis, atelectasis, and pulmonary and bronchial infections as a result of aspiration of esophageal contents, all factors thought to be necessary for the development of bronchiectasis are also present.

Therapeutically the early institution of measures enhancing esophageal emptying so that aspiration of retained contents into the lungs is prevented may be of considerable value.

T. LAUCURIA, M.D.

Taylor J W: Spontaneous Lobectomy *Brit. M. J.*, 1944, 2 500.

It has become increasingly difficult to differentiate between a lung abscess and an empyema. In many

cases the infection is primarily in the lung tissue and invades the pleural cavity only secondarily. This has given rise to the term 'pleuropulmonary abscess'. In the following case the infection was so great that the lung slough of the complete upper lobe became free in an empyema cavity.

The illness began with an attack of lobar pneumonia, which was followed by a period of recovery. This was interrupted by an excessive cough, productive of thick greenish yellow sputum, and accompanied by symptoms of malaise and pyrexia. Clinical examination some two months later suggested an empyema, and drainage was indicated. At this time the cough was noted to be positional, the patient coughed more when he was upright than when flat in bed. The presence of Friedländer's bacillus in the pus from the cavity was a rare and unexpected finding. The skin and subcutaneous tissue in the right upper chest were infiltrated with 0.5 per cent penicillin, and aspiration of the chest in the sixth interspace in the midaxillary line produced pus.

A portion of the sixth rib was removed and the parietal pleura was opened. A large apical cavity was entered and 45 oz. of thick green pus was withdrawn. During a violent fit of coughing a slough of the whole of the right upper lobe was expelled from the wound and followed by a gush of foul-smelling pus. A large drainage tube was inserted into the cavity, the skin was lightly sutured and a light dressing was applied. The lung slough measured 30 by 8 by 6 cm. It had a gray ragged appearance and was pitted with small holes.

Removal of the tube six months after drainage was started still left a cavity in the right upper zone. This cavity was draining into a patent bronchus on its lower and medial aspect. Up to this time the presence of the cavity has not given rise to any symptoms. The question of an apical thoracoplasty must, however, be kept in mind, so that the cavity may be closed completely if it should again give rise to any symptoms.

CHARLES BAROCK, M.D.

Cheale, J. M., and Young, F. H.: The Prognosis after Successful Pneumonectomy. *Lancet* Lond. 1944, 247-254.

Pneumonectomy is being performed with increasing frequency. There has until recently been little dependable evidence on which to estimate the post-operative hospital stay, the time elapsing before patients could resume work, and the capacity for normal life and work.

The authors studied the cases of 25 patients operated upon between 1935 and 1940 who had survived the operation at least once year. The symptom which most often keeps the patient with a surgically successful case from gainful occupation is dyspnea on mild exertion. A simple test was adopted to gauge this factor: the degree of dyspnea produced by walking upstairs from the ground to the first floor of an ordinary house. It was believed that if this could be done without dyspnea the patient could lead a useful life. It is also important to

realize that a bronchial fistula is the determining factor in the length of stay in the hospital and the length of time before work can be resumed.

In the series studied by Cheale and Young the average stay in the hospital was fifteen weeks. In the cases of 13 patients gainfully employed, the average time since operation was eleven months. (When there is no bronchial fistula this period can probably be halved.)

Only 1 patient reported dyspnea at rest—a six-year-old child. On the stairs test 15 reported they were not short of breath, 7 were slightly and 2 were definitely dyspneic. The younger the patient, the less marked was the shortness of breath.

J. M. Mora, M.D.

White, W. L., Burnett, W. E., Bailey, C. P., Rosemond, G. P., and Others: Penicillin in the Prevention of Postoperative Empyema. *J. Am. M. Ass.* 1944, 26-6.

Most attempts to measure the potentialities of a drug in wound infections, whether in terms of prophylaxis or of treatment, suffer from extreme degrees of variations in the lesions studied. The wound variations occur in respect to size, depth, anatomic location, infecting agents, degrees of contamination, types and numbers of organisms present, and the amount of contained foreign matter. Wounds also vary with the individual patient as to age, concomitant disease, nutrition, individual host resistance, and healing capacity. Still another source of variation is the management of the wound, the length of time that has elapsed between injury and definitive treatment, the extent of debridement and of wound closure, the degree of tension in closed wounds, adequacy of immobilization, frequency of dressings, and the duration of hospitalization. In established infection all of these variables are present, plus the factors of bacterial invasion, bacterial toxins, and bacterial symbiosis, which further complicate the picture. Hence, it is considerably more difficult to assess the efficacy of a drug in surgical infections than in the more uniform non-surgical diseases such as pneumonia, cerebrospinal meningitis, or gonorrhea, in which factors relating to the presence of a wound are nonexistent.

This study was designed to minimize the factors of variation, to offer adequate and comparable controls, and to provide a clearly definable end-point as the basis for evaluating the agent. Therefore, the objective of these authors could be simply stated as follows: To determine if penicillin is of value in the prevention of empyema following transection of the bronchi.

The effect of penicillin as a means of preventing postoperative infectious complications after lobectomy and pneumonectomy was so clearly demonstrated in 40 experimental and control cases that it was not believed justifiable to continue the use of controls. The frequency of hemolytic streptococcal empyema in control cases probably accounts for much of the success obtained with the use of sul-

foamades in recent years. The occurrence of post operative empyema in all control cases of lobectomy pneumonectomy, and bronchiectatic and lung abscess is very striking when compared with the absence of postoperative infection in the cases receiving penicillin.

The preoperative administration of penicillin has been a most important feature of this study. The drug given during this period probably serves to control acute and chronic infection in the pulmonary tissues, which reduces the possibilities of postoperative infections. In addition the preoperative use of penicillin affords a maximum therapeutic effect at the time the pleural space is exposed to bronchial contamination.

Penicillin administered by intramuscular injection for one week preoperatively and two weeks post operatively in doses of 150,000 units daily appears to be useful in preventing postoperative pyogenic infections following lobectomy or pneumonectomy.

Penicillin is apparently of no value in preventing or controlling tuberculous infections.

JONAS E. KIRKPATRICK, M.D.

ESOPHAGUS AND MEDIASTINUM

Ladd W. E., and Scott H. W. Jr.: Esophageal Duplications or Mediastinal Cysts of Enteric Origin. *Surgery* 1944, 16: 815.

The authors report 5 cases of mediastinal cysts of enteric origin from the Children's Hospital of Boston, Massachusetts. These cysts are more properly called "esophageal duplication" since they actually arise from or are adherent to, the esophagus. In 4 of the 5 cases, the muscularis layer of the esophagus may be continuous with the wall of the cyst. In 1 of the cases, however, no attachment to the esophagus was found.

These enteric duplications are found early in life, the youngest patient being three weeks of age and the oldest twenty-two months of age. The oldest recorded patient in the literature was a boy three and one-half years of age. Both sexes are equally involved.

The symptoms caused by these duplications are those of an enlarging mediastinal mass producing pulmonary or esophageal compression such as cough, dyspnea, cyanosis, recurrent pneumonias, dysphagia or regurgitation of food. Pain may also be a feature, due apparently to increased intracystic pressure. Hematemesis and hemoptysis have both been observed in these patients and is due to the diminution of the blood supply to the bronchial or esophageal mucosa with subsequent sloughing. Peptic ulcer may occur in the mucosal lining of these duplications.

The roentgenological examination shows a mediastinal mass situated posteriorly. It is usually spherical due to the fluid content. The heart and mediastinal structures may be displaced. Bronchograms may show pulmonary compression but no connection with the enteric duplication. Likewise esophageal

examination with contrast media shows no actual fistulous connection between the duplication and the esophagus itself. Occasionally a vertebra or rib may show erosion from pressure.

These cystic structures are of variable size and may be situated anywhere along the entire length of the mediastinum. They expand either into the left or right hemithorax. The walls are rather thick and the lining is mucous membrane. They often have two muscular layers resembling the esophagus. The mucosa may be that of the esophageal or gastric type. No serosa is present but the pleura which overlies the mass may be mistaken for it. These masses are always retropleural. In 4 of 5 of the cases the mass was attached to the esophagus; in fact, it could not be separated from this organ. The layers of the mass may blend with those of the esophagus. No fistulous connection between the mass and the esophagus was found either at operation or at autopsy.

The contents of these cysts resemble the gastric juice and positive reactions for pepsin and rennin may be obtained with tests. In addition, high titers of hydrochloric acid may be encountered.

The various theories regarding the embryological aspects of this anomaly are discussed.

Treatment consists of excision of the mass if possible. It is usually found, however, that the mass cannot be completely removed without serious injury to the esophagus. In fact, it is often a very sessile attachment. If it cannot be completely removed it is marsupialized and packed with gauze or other coarse packing to allow the mucosal lining to slough or some sclerosing solution may be injected into the cyst after marsupialization. Curettage of the exteriorized sac was done in 1 case with satisfactory results and the sinus tract healed and obliterated itself.

Two of the 5 patients observed died but the other 3 recovered. The oldest child has now been followed up for sixteen years and there is no disturbance of the anatomy or physiology of the thorax.

FORREST D. DODGILL, M.D.

MISCELLANEOUS

Ferguson C. F. and Neuhauser E. B. D.: Congenital Absence of the Lung (Agenesis) and Other Anomalies of the Tracheobronchial Tree. *Am J Roentg* 1944, 53: 459.

Only about 50 cases of congenital absence of the lung have been recorded in the medical literature. In 6 of these diagnosis had been made before death.

The authors, during the past six years, observed at the Children's Hospital of Boston, Massachusetts 5 cases of agenesis of the lung, all of which were diagnosed during life by bronchoscopy and lipiodol roentgenography. One of the patients died and autopsy confirmed the clinical diagnosis. The remaining 4 enjoy apparently normal lives.

A review of the literature reveals that agenesis of the lung occurs with preference on the left side and is encountered more frequently in males than in females.

males. In the authors' series the absent lung was found on the left side in 3 cases, but 3 patients of the 5 were females.

Various theories have been propounded to explain this developmental anomaly. Since the condition often is associated with other congenital defects, a developmental error of endogenous origin in the germ plasma constitutes probably the most logical cause. The associated defects, according to the literature include narrowed trachea, extracartilaginous rings, supernumerary bronchi of the normal lung, absence of the pleura on the affected side, tracheo-esophageal fistula, esophageal stenosis, synostosis of various ribs, absent diaphragm on the affected side, atresia of the anus, hypoplasia of the face, absence of one ovary and tube, agenesis of the spleen, kidney and ureter, exencephaly and absent vagus nerve. Each of the authors' 5 patients had some other anomaly such as harelip and cleft palate, absent hand and wrist on the affected side, defect of the external ear and other minor congenital defects.

Schneider differentiates 3 anatomic subdivisions of agenesis of the lung: (1) true aplasia, cases in which there is no trace of a lung, bronchus, or vascular supply on the affected side, (2) cases in which there is a primordial bronchial bud but no lung tissue and (3) extreme hypoplasia, cases in which the bronchus is fully developed, but reduced in size and ending in a fleshy structure without lobes which lies in the mediastinum. Two of the authors' 5 cases belonged to group 1 and 3 to group 2. The third group is very rare, only 5 such cases having been reported in the entire literature.

No symptoms are noted in many cases of agenesis of the lung and the condition is discovered accidentally as happened in some of the authors' cases during physical examination of otherwise essentially normal children. If however, symptoms are present, they may be very variable and inconsistent. Positive physical signs include diminished respiratory excursion, slight flattening of the thorax with possible scoliosis, dullness or flatness to percussion and absent breath sounds or bronchial breathing. In practically every case, the potentially vacant space is filled with heart, displaced mediastinal contents, or fluid.

The clinical examination very often leads to an erroneous diagnosis of pneumonia, massive atelectasis, foreign body in the bronchus, hydrothorax, diaphragmatic hernia, or diaphragmatic paralysis. However from a roentgen study of the chest the condition may be suspected. There is a dense homogeneous shadow on the affected side with displacement of the heart and mediastinal contents, elevation of the diaphragm, and narrowing of the intercostal spaces. Bronchoscopy is, then, the final method of accurate diagnosis especially if followed by lipiodol injection of the tracheobronchial tree. The authors briefly present the case histories in their 5 patients, accompanied with the respective roentgenograms and bronchograms.

The prognosis is guarded but not incompatible with longevity. The oldest patient in the author's series is over eight years of age. Three of the patients reported in the literature lived well over fifty years.

T. LEVOTINA, M.D.

SURGERY OF THE ABDOMEN

GASTROINTESTINAL TRACT

Palmer W. L. and Humphreys E. M.: Gastric Carcinoma. Observations on Peptic Ulceration and Healing. *Gastroenterology* 1944 3 357

Here again is presented evidence that certain ulcerating gastric carcinomas may present the architectural characteristic of peptic ulcer and that such ulcers may in fact heal and the scar be covered by neoplastic mucosa or by a layer of epithelium perfectly normal in appearance.

The first patient, forty years of age, had suffered some months previously with symptoms vaguely suggesting peptic ulcer which had improved under ulcer management and then presented roentgenologically a small penetrating gastric ulcer with maximum (histamine) free acidity of 106. At autopsy two months later a lesion about 1 cm. in diameter and from 1 to 3 mm. deep was found grossly this lesion appeared to be benign. However microscopic examination disclosed frank carcinoma in the mucosa on both sides of the ulcer and growing over the base in some places. Extending laterally from the ulcer into the mucosa was a linear slightly depressed and puckered scar up to 1 cm. wide and 4 cm. long apparently lined with mucosa. In this scar were noted the fusion of muscularis mucosae and muscularis propria and the complete re-epithelialization of a healed ulcer but there were definite neoplastic cells in this epithelium and beneath the muscularis mucosae.

The second patient a male of fifty-six years had shown symptoms (attacks of hematemesis and tarry stools gnawing epigastric pains high free acidity) and x ray evidence of a large penetrating ulcer high on the lesser curvature of the stomach with gas roentgenologically "tremendous hypertrophic gastritis of the whole stomach suggestive of extensive neoplastic infiltration. His condition improved rapidly on ulcer management with a marked decrease in the size of the ulcer as shown roentgenologically. However a year later this ulcer was still present although small and a new ulcer was found in the prepyloric region of the antrum. The latter ulcer disappeared roentgenologically and then reappeared. Autopsy some weeks later disclosed a diffusely infiltrating carcinoma of the stomach with pyloric obstruction, carcinomatous peritonitis, healed gastric ulcer in the prepyloric region and chronic in active ulcer high on the lesser curvature. Three centimeters from the esophageal junction and 15 cm. from the lesser curvature on the posterior wall of the stomach there was a defect in the mucosa 8 mm. in diameter. This ulceration showed a cleanly sloping wall and a firm grayish-white base with considerable scarring and stellate contraction. There was another irregularly depressed scarlike area on the lesser curvature about 3 cm. from the pylorus.

The architecture of the ulcer high on the lesser curvature and the high gastric free acidity again may both be interpreted as evidence in favor of the initial benign nature of the lesion although the course speaks strongly against this view. The ulcer disappeared and recurred but at autopsy it was found to be healed. Here as in case 1 the regenerated mucosa contained neoplastic cells.

Case 3 was that of a carpenter seventy-one years of age, with a low free acidity (26 with histidine) but otherwise with a rather typical ulcer history for about three years. Occult blood (benzidine test) was persistently present in the feces in varying amounts and roentgenography and gastroscopy disclosed a "craterlike big ulcer" of the lesser curvature which under ulcer management decreased markedly in size while the occult blood persisted but later the ulcer increased in size again and in the resected specimen it was found to be 10 by 15 mm. in diameter surrounded by an edematous hyperemic mucosa which was microscopically adenocarcinoma.

Case 4 was that of an unmarried female forty-one years of age, who had been suffering for about two years with pain of the ulcer type which was relieved by eating and by taking soda. Roentgenography disclosed a crater on the lesser curvature with radiating polypoid folds and a tendency toward annular constriction of the antrum. Two months later under ulcer management the ulcer had disappeared roentgenologically but the abnormality of the wall was still evident. However a month later the crater was again faintly visible and although it was decreasing progressively in size it was always visible gastroscopically surrounded by a stiff infiltrated nodular area. When the resected specimen of stomach was opened there was disclosed an area on the lesser curvature from which the mucosal folds radiated outward. The lesion was firm, not hard and the borders were very slightly raised. At the center were two small ulcerated areas each measuring 1.0 by 0.6 cm. by 1 mm. deep, with a smooth floor. The remainder of the lesion was covered by soft pink tissue similar to but slightly pinker than the surrounding mucosa. In spite of the two-year story of periodic distress of the ulcer type there was nothing pathological to suggest the previous existence of a benign peptic ulcer. There was on the other hand evidence of peptic ulceration in a neoplasm and of subsequent healing with a layer of normal-appearing well polarized simple epithelial cells covering fresh granulation tissue and the underlying tumor.

Excellent photographs accompany the article.

In the discussion EUSTERMANN of Rochester, Minnesota states that about 10 per cent of gastric carcinomas masquerade as benign gastric ulcer and that some carcinomatous lesions occasionally respond to treatment so favorably that their malignant nature is not suspected.

FITZGIBBON of Portland Oregon reports a gastroscopically diagnosed gastric ulcer which under ulcer management at the end of one and one-half months was healed and completely covered with mucosa, with the puckered appearance that one might expect from a scar. Later however it exhibited gastroscopically an extensive carcinomatous involvement. At operation involvement of the posterior wall and lesser curvature with lymph node and liver metastases was found.

CROWN of New York says that he did not realize, until he heard Palmer speak, that a malignant ulcer might "heal" and become covered by epithelium. However the healed malignancy is covered not by a normal epithelium, but by malignant carcinomatous epithelium. The malignant ulcer never heals completely.

RUFFIN of Durham, N. C. asked the speaker if he subscribes to the aphorism "Carcinomas may ulcerate but ulcers do not carcinoma." Palmer replied in the affirmative. JOHN W. BRIDGMAN, M.D.

ILLINGWORTH, C. F. W., SCOTT, L. D. W., and JAMIESON, R. A. Acute Perforated Ulcer in the West of Scotland. *Brit. M. J.* 1944 67

To ascertain the incidence of perforated ulcer in the twenty year period from 1924 to 1943 records were obtained from the three main Glasgow voluntary hospitals the Royal, Western and Victoria Infirmaries. The number of perforations treated annually increased rapidly in the period under review. In the prewar years there was a fairly uniform increase from rather less than 200 in 1924 to rather more than 400 in 1938. During the war the number of perforations was higher in 1940 and 1941 and lower in 1942 and 1943 than would have been expected on the basis of the trend in the previous sixteen years both the excess and the deficiency are statistically significant. It should be added that these changes are not due to wartime changes in the population. The incidence of perforation per 100,000 from 1924 to 1938 follows:

Year	1924	25	26	27	28	29	30	
Incidence								
Per 100,000	11	12	16	17	19	20	19	
Year	193	32	33	34	35	36	37	38
Incidence								
Per 100,000	20	30	19	23	22	22	25	

The author reviewed the incidence of perforations during the present war with special reference to air raids. In London the rising incidence was noted shortly after serious air raids began (in September, 1940) and a similar correlation was noted in Bristol and Liverpool. So far as Glasgow is concerned however a close study of the figures leads to the conclusion that such a correlation did not exist. In Glasgow the incidence rate began to rise in the autumn of 1940 reached a high peak in March 1941 and remained abnormally high until the end of June, 1941. However in Glasgow the rise in incidence did not follow air raids on the contrary it anticipated them. In Glasgow there was nothing comparable to

the prolonged bombardment to which London was subjected. Apart from a few desultory raids, which excited greater interest than apprehension, the first attacks to be sustained were the two heavy raids in March, 1941. These raids occurred on March 13 and 14 and March 14 and 15 but the high incidence of perforations in March cannot be attributed to them, for of the 86 perforations recorded in March no fewer than 41 occurred before the air raids began. From these observations it is clear that in Glasgow the local air raids cannot be held responsible for the 1940 and 1941 increase of perforations and other factors must be considered. During the period in question the whole country was in a state of nervous strain as a result of the war situation. From the summer of 1940 onward, also there was a great increase in the amount of overtime work, and there were additional duties in connection with the Civilian Defence Services and the Home Guard the resulting weariness, lack of sleep, and irregularity of meal hours might well be tolerated for a few months but might later precipitate perforation. Finally it is possible that the food shortage which was beginning to be evident at that time may have exerted an influence. The fall of incidence after June 1941 and in 1942 and 1943 is equally interesting and even more difficult to explain. It could be suggested that ulcer patients who might have experienced perforation in 1942 or 1943 had already done so in 1941 but this explanation will not do for one perforation does not protect against subsequent ones. There is indeed no ready explanation of this fall in incidence.

In sex distribution a great preponderance of males is evident and the overall ratio of males to females is 6,796 to 360 or 19 to 1. The incidence rate of perforations increased in both sexes throughout the twenty year period, and the ratio of 19 to 1 was substantially maintained although there were wide fluctuations from year to year. The rise in 1940 and 1941 and the fall in 1942 and 1943 were confined to males. In females the general trend of the prewar years was maintained. This finding is somewhat surprising in view of the great changes which have taken place in the habits and working conditions of women, especially since 1930.

The general characteristics of the age distribution showed that the incidence reaches its maximum in patients between thirty-five and forty five years of age and falls only slowly in older patients. An interesting feature was the sudden increase in the frequency of perforation at adolescence. Perforation in childhood is rare. There was 1 perforation at eight years, 1 at eleven and 1 at twelve years. From age thirteen to nineteen there is a truly remarkable increase, the numbers observed at the successive single years of age being 1, 6, 6, 32, 44, 86, 101. The age distribution did not remain stable throughout the period. Between 1924 and 1933 the mean age rose by some three and one-half years, the rate of increase being fairly uniform. The rise was doubtless due in part to the increasing mean age of the popu-

lation in the area served. There was a small but nevertheless real difference in age incidence in the two sexes.

CHARLES BARON M.D.

Mingworth, C. F. W. Scott, L. D. W. and Jamieson, R. A.: Acute Perforated Peptic Ulcer in the West of Scotland. *Brit. M. J.* 1944, 2: 655

The authors have reported figures relating to the incidence of perforated peptic ulcer over a twenty year period in an area of western Scotland with a population of over two million inhabitants.

From 1924 to 1938 there was a progressive increase in the incidence of perforations. During the period of the war this steady increase has been interrupted by a marked rise during 1940 and 1941 followed by a return to a lower level. These changes concern duodenal ulcer almost entirely the incidence of which far exceeded that of all other types of ulcer. The total number of cases was 3,882. Of these 493 (12.7 per cent) were gastric ulcers, 3,220 (82.95 per cent) were pyloroduodenal ulcers, 52 (1.34 per cent) were anastomotic ulcers, the location of 117 (3.01 per cent) was not stated. The rise in incidence during 1940 and 1941 was not correlated with air raids in this part of the country but it is suggested that in addition to anxiety about the war situation, overwork and perhaps undernutrition may have exerted some influence.

The sex ratio has undergone little change during the twenty year period. The rise of incidence in 1940 and 1941 and the fall in 1942 and 1943 were confined to men. In women the general prewar trend was maintained during the years of war. This finding is somewhat surprising in view of the great changes that have taken place since 1939 in the habits and working conditions of women. There is a predominance in males of perforations of all types. The sex difference is particularly striking in anastomotic ulcers, all of which occurred in males. There is a difference in the sex ratio of gastric and duodenal perforations. In males, 12 per cent of perforations were gastric and 83.6 per cent were duodenal the comparable figures for females were 25 per cent and 70.6 per cent. Statistical analysis shows that it is highly improbable that the difference in sex ratio has arisen just as a matter of chance.

Perforation occurs rarely during childhood its incidence rises rapidly in adolescence and attains a maximum between the ages of thirty and forty years. Since 1924, there has been a rise in the mean age which does not appear to be due entirely to aging of the population. The mean age is higher in females than in males.

Perforations are unduly common in the month of December and relatively uncommon in the months of August, September and October. This low incidence in the summer months may possibly have a nutritional basis, or may be related in some way to the summer holiday season. Perforations occur less frequently on Sundays and Mondays than on other days, and this may be related to rest over the week end. Perforations are unduly common between the

hours of three and six o'clock in the afternoon and comparatively uncommon during the night and morning. The relation of these phases to meal times is not clear and requires further study. There may be a correlation with periods of stress and rest respectively.

The fatality rate from perforation increases with age and with delay in treatment. It is greater in gastric ulcer than in duodenal ulcer in females than in males, and in winter than in summer. The last may well be attributable to the increased risk of pulmonary complications in the winter months.

CHARLES BARON M.D.

Warren R. F. Primary Malignant Tumors of the Small Bowel. *Cases of Am. J.* 1944, 51: 451

Although primary malignant neoplasms of the gastrointestinal tract are extremely common there is a surprising variation in their incidence between the pylorus and the ileocecal valve. The author presents 26 cases as follows:

Adenocarcinoma in the first part of the duodenum	0
Adenocarcinoma in the second part of the duodenum	4
Adenocarcinoma in the third part of the duodenum	1
Adenocarcinoma in the duodenojejunal junction and jejunum	11
Adenocarcinoma in the ileum	1
Total	17
Sarcomas	4
Carcinoids	4
Primary Hodgkin's disease of the small bowel	1
Total	26

The series supports the claim that duodenal malignant disease tends to occur most frequently in the periampullary region. The onset of a painless jaundice which is said to characterize malignant change was seen in only 1 case. Three of the 4 patients gave a history of a year or more of gastrointestinal upsets which were suggestive of ulcer or cholelithic indigestion.

Adenocarcinoma of the small intestine exclusive of the duodenum is said to make up 3 per cent of intestinal cancers according to Ewing. This suggests a slightly greater frequency of duodenal cancers than of jejunoileal cancers. This is not borne out by the author's series in which the ratio is 5 to 12.

Carcinomas tend to develop at the extreme upper and lower ends of the small bowel and leave the central portions free. This was shown in this series by the occurrence of 11 carcinomas in the jejunum or duodenojejunal junction, and 1 in the terminal ileum.

Less common than adenocarcinoma is sarcoma, which is found more often in the small than in the large bowel. This series included 4 cases about 14 per cent of the total made up of 1 sarcoma of uncertain cell type, 1 reticulum-cell sarcoma, 1 malignant melanoma and 1 leiomyosarcoma. All 4 cases in

volved the ileum and thus conformed to the accepted view that sarcomas of the small bowel occur most frequently in the ileum.

Four carcinoid tumors or 14 per cent of the total series are reported. Usually these arise in the appendix and may not be recognized at the time of operation. Nevertheless they occur with considerable frequency in the small bowel usually the ileum and have been reported in the stomach and colon. Were it not for incidental cases picked up at routine autopsy few if any of these not infrequent tumors would be discovered.

Finally, 1 case of Hodgkin's disease of the small bowel was included.

The 17 cases of adenocarcinoma were divided equally between the sexes. The age incidence for the males was sixty and eight-tenths years, while that of the females was fifty three and five-tenths years.

The symptoms in many cases were of long standing. One patient had twenty years and another twenty seven years of gastrointestinal upsets. Symptoms are nearly always referable to mechanical obstruction. The tumor may be one of three types (1) that which engirdles and strangles the bowel (2) that which by its fungating massive growth obstructs the lumen, and (3) that which by a process of low infiltration finally brings about stricture of the lumen. Pain is not characteristic until obstruction supervenes. The symptoms may be divided into those of long-standing irritation and those of the acute obstructive phase. Occasionally there are tarry or bloody stools. The obstructive phase includes nausea and vomiting, jaundice (especially in carcinoma of the second part of the duodenum), loss of weight, loss of appetite, and increasing constipation.

The prognosis is poor. There are usually metastases when the patients are admitted. 11 of the 17 in this series had metastases and 9 died in the hospital. Of those that left the hospital 5 died within two years. For carcinoid tumors the outlook is much brighter. The rarer sites for these tumors are known to signify more malignant cases.

STEPHEN A. ZEEMAN, M.D.

Shallow T. A., Eger S. A. and Carty J. B.: Primary Carcinoma of the Third Portion of the Duodenum. *Surgery* 1944, 6: 939.

Primary carcinoma of the small intestine is a comparatively rare lesion and extremely so when in the third portion of the duodenum. Since an opportunity seldom arises for radical resection of such a lesion, there being only 12 unquestionable cases reported, the authors describe a case in which a new operative procedure was successfully employed its advantages are discussed, and details of the other resected cases are tabulated.

A sixty-three year-old white man had been in excellent health until one year prior to admission to the hospital, when epigastric fullness occurred about one half to one hour after meals, and remained for several hours unless relieved by belching. No par-



Fig. 1. Anatomic relationship of tumor represented diagrammatically. Lines A and B are sites of resection.

ticular type of food brought on an attack, which occurred every four to six weeks at the onset but gradually increased in frequency and severity. For two weeks prior to admission epigastric distress and fullness were constant, and were relieved only by vomiting. The vomitus was bile stained and contained particles of food ingested several meals previously but it never contained blood. There was a loss in weight of 20 pounds during the last six months, and most of this occurred in the last two weeks.

Abnormal findings consisted of mild dehydration, moderate epigastric distention and a deep, firm, fixed nontender mass 3 inches in diameter just above the umbilicus. The gastric contents contained a residual total acidity of 35 and free hydrochloric acidity of 20. After a test meal these figures gradually rose to a maximum of 48 and 27 respectively, in the sixth specimen. There was bile present in all the specimens but blood and lactic acid were absent.

Röntgenographic study of the gastrointestinal tract demonstrated almost complete obstruction at the beginning of the ascending loop of the duodenum. The diagnosis made was a lesion in the third portion of the duodenum probably due to a malignancy either primary or secondary.

After the patient was transferred to the surgical service operation was performed on August 4, 1943. A tumor was found involving the posterolateral wall of the third portion of the duodenum beneath the superior mesenteric vessels. The adjacent retroperitoneal tissue was indurated, but there was no evidence of extension of the growth or metastases. The entire third portion of the duodenum was mobilized and resected. The free ends of the bowel were closed. An antecolic duodenojejunostomy was performed in a side-to-side manner to anastomose the jejunum, about 10 inches from the ligament of Treitz, to the second portion of the duodenum, just

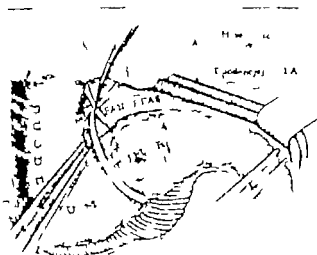


Fig. 1. Third portion of duodenum and duodenojejunal angle mobilized prior to resection. Dotted line on second portion of duodenum represents site for side-to-side duodenojejunostomy.

distal to the ampulla of Vater. The suture line of the closed duodenal stump was reinforced by anchoring it to the posterior surface of the jejunum just distal to the anastomosis. The jejunal stump was attached to the ligament of Treitz to leave the proximal jejunum available for a gastroenterostomy should the duodenojejunostomy stoma have proved inadequate. The abdomen was closed without drainage.

The histological diagnosis was primary ulcerative adenocarcinoma of the duodenum. Nine months after operation the patient was symptom-free, had gained 30 pounds in weight, and x ray examination following a barium meal revealed no kind of abnormality.

The authors have been able to collect from the world literature reports of only 12 unquestionable cases of primary carcinoma of the third portion of the duodenum in which resection was done. The procedure employed by the authors has the following advantages:

1. The anastomosis is safer for it is performed where the duodenum has a peritoneal covering.
2. The closed duodenal stump is reinforced by being buried in the under surface of the distal jejunal loop.
3. With the side-to-side anastomosis the angles can be well fortified and the size of the stoma regulated without encroachment on the common bile duct, ampulla of Vater or the blood supply of the remaining duodenum.
4. With the jejunum antecolic, obstruction from pressure by the superior mesenteric vessels and from the passage through the transverse mesocolon is avoided.
5. A proximal jejunal loop is provided for a gastrojejunostomy should the duodenojejunostomy stoma prove to be inadequate.

JOSEPH K. NARAT, M.D.

Woods, F. M. and Hanlon, C. R. Inflammatory Stricture of the Rectum: An Analysis of 192 Cases, Including 35 Treated by Rectosigmoid Resection. *Ann. Surg.* 1944, 120, 598.

The treatment of inflammatory rectal stricture has long been unsatisfactory. The causal relationship of lymphopathia venereum to rectal stricture is now generally conceded, but there is no such unanimity of opinion regarding treatment. There are many reasons for this difference of opinion.

First, the strictures vary from simple fibrous narrowings causing no symptoms to extensive lesions involving the rectum and colon with partial or complete obstruction.

Second the presence of ulcerations, sinuses and fistulas may complicate the problem.

Finally the degree of co-operation of the patient will determine management. Measures involving repeated clinic visits, prolonged administration of drugs or observance of careful hygiene are generally not employed successfully in such patients as form the bulk of the authors' practice.

The various modes of attack on inflammatory rectal stricture may be grouped conveniently under four headings: (1) drugs and antigens, (2) irradiation, (3) dilatation and (4) surgery.

With asymptomatic stricture, insistence on careful hygiene and regulation of the bowels may be sufficient. Patients have been followed for as long as twenty years in this series without appreciable progression of symptoms.

With strictures showing evidence of inflammatory activity or intestinal obstruction, more active treatment is necessary.

This may consist of sulfonamides with which good results have been reported both in the early stages of the disease and in secondary infections. The authors have not seen the resolution of firm fibrous strictures as reported by some authors.

Antigen therapy has been recommended for all forms of the disease but published reports offer little encouragement for treatment of rectal stricture by this method. The authors' experience with antigen therapy has been negligible.

Dilatation has been widely used. It affords temporary relief of obstructive symptoms in the great majority of patients although the risk of exacerbating the infection or perforating the bowel is commonly recognized. The authors' experience includes 7 deaths attributable to this procedure.

With an inflammatory rectal stricture that does not respond to conservative measures, colectomy may be expected to eliminate obstruction and in many patients to mitigate the inflammatory symptoms. Forty-one per cent of the authors' patients were benefited by simple colectomy. In comparing this result with that in the resected cases of which 94 per cent were improved, one should recall that a higher percentage of 'severe' cases were subjected to simple colectomy. This may account partially for the 'poor' results in the latter group.

Several authors have reported radical removal of the diseased rectosigmoid usually by perineal resec-

tion. Failures following this operation may be attributed to extension of the disease beyond reach of the perineal approach. The only "poor" results in this series of resections occurred with the perineal approach because of persistent drainage from the perineum or from the distal colostomy loop. Twenty-three combined abdominoperineal resections of which 16 were in one stage, gave quite satisfactory results. Certain of these cases might have been managed with equal success by less radical methods. In the majority, however, the rapid restoration of the chronically ill patient to good health apparently justified such drastic treatment.

JOSEPH GASTEL, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Berman C.: The Clinical Features of Primary Carcinoma of the Liver. *Clin. Proc., Cape T* 1944 3 333

Primary carcinoma of the liver is a problem of major importance to South African medicine, because it occurs with appalling frequency in most pigmented races. In Europe however it is one of the rarest of tumors. Among the Bantu and Javanese males, particularly it is undoubtedly the most frequent form of carcinoma. While the postmortem rate is 0.13 per cent in Europe and 0.25 per cent in America among Asiatic races it is 1.3 per cent for the Javanese, 1.21 per cent for the Japanese, 1.9 per cent for the Chinese, and 1.44 per cent for the Philippine Islanders. For the African Bantu it is 1.2 per cent. Again, while the percentage frequency of primary liver cancer to all other forms of cancer is 1:1 per cent in Europeans and 2:1 per cent in Americans, it is 36:3 per cent in the Javanese, 36:1 per cent in the Chinese, 2:1 per cent in the Philippine Islanders, 7.8 per cent in the Japanese and 25.3 per cent in the Bantu.

There are no symptoms which are pathognomonic of primary carcinoma of the liver. Nevertheless, if the clinical manifestations are taken collectively ample evidence is furnished from which a correct diagnosis can be made. Primary liver cancer is predominantly a disease of males. In the Bantu it occurs chiefly in young adults. Elsewhere, however it is commonest in or after middle age. Cirrhosis occurs with such regular frequency in primary liver cancer that many pathologists regard it as an intermediate stage in the neoplastic evolution, especially as numerous known cirrhotic agents have frequently been discovered in close association with liver cancer. Among these are intestinal parasites, malaria, schistosomiasis, distomatiasis, echinococcus infestation, and hemochromatosis.

Since Sasaki and Yoshida first produced primary liver cancer in rats by feeding them with the hydrocarbon α -aminonaphthalene no organ has yielded more spectacular results in the experimental production of cancer than the liver. Other related chemical compounds, like p -dimethylaminonaphthalene (but

ter yellow) are today producing liver cancer with even greater ease.

A study of 66 Bantu cases of primary liver cancer has indicated that the clinical course of the disease is by no means uniform. The symptomatology is dependent upon the rate of neoplastic growth, complications, and metastases. Accordingly, the author has divided his cases into five clinical groups as follows: (1) frank cancer i.e. with symptoms of primary liver involvement (63.6 per cent of cases) (2) acute abdominal cancer i.e. with symptoms associated with an acute abdominal catastrophe (9.1 per cent) (3) febrile cancer i.e., with fever as the salient clinical feature (7.6 per cent) (4) occult cancer, in which malignancy is discovered accidentally (15.1 per cent) and (5) metastatic cancer with symptoms referable to the organs involved by metastases rather than to the liver (4.6 per cent of cases).

The diagnosis is based upon clinical findings together with microscopic examination of pathological material obtained at operation or biopsy. Roentgenological examination is of value in suspected "metastatic" cancer. Verification of the diagnosis, however is often established only at autopsy. All liver function tests devised thus far including the galactose test and the bromsulphalein test are of doubtful value. Recent work has indicated however, that the Takata-Ara test may be of value in the diagnosis. This is a flocculation test of serum with a mixture of sodium carbonate and mercuric chloride.

The following diseases must be considered in the differential diagnosis.

In frank primary liver cancer—neoplasms of the pylorus, transverse colon, pancreas or right kidney including their metastases to the liver; cirrhosis, syphilis, chronic venous congestion, or cystic disease of the liver; cholelithiasis, abdominal tuberculosis, leucemia, Banti's disease and amyloid disease.

In acute abdominal cancer—volvulus of the small intestine, perforated gastric, duodenal or umbilical typhoid ulcer, ruptured liver or spleen, biliary or renal colic, acute appendicitis, acute pancreatitis and mesenteric thrombosis.

In febrile cancer—abscess, liver abscess, intrahepatic suppuration, hydatid cyst of the liver, malaria, and subphrenic abscess.

The outlook is hopeless as the disease is rapidly fatal. Indications of approaching death are sudden marked enlargement of the liver, rapidly intensifying jaundice, increased dilatation of the superficial abdominal veins and additional edema of the extremities.

Because of the hopelessness of the disease, treatment is essentially palliative and is directed toward the relief of pain and discomfort. Sedatives are always required in large and increasingly frequent doses. The question of surgical treatment must be considered. In the author's own cases, however all attempts at radical cure had to be abandoned on account of metastases in other parts of the liver. Reports in the literature, too, indicate that operative

results have been very poor. It is possible that x-ray and radium therapy may prove of value in treatment. The author has been unable to study the effects of these methods because of the lack of facilities.

JOSEPH K. NARAY, M.D.

Brush, B. E. and McClure, R. D.: Hyperinsulinism Treated by Subtotal Pancreatectomy. *Iowa Surg.* 1944 120-750.

Functional hypoglycemia is fairly common but organic hyperinsulinism is rather rare. It is of utmost importance to study every diagnostic aid available in order to establish an etiological diagnosis of hypoglycemia.

The Whipple triad of symptoms is a definite indication for surgical exploration of the pancreas. An islet tumor will be present in nearly all of the cases. The Whipple triad includes (1) disorders of the nervous system such as confusion, coma, convulsions collapse coming on in the fasting state; (2) a drop in the blood sugar level to 50 mgm. per 100 cc. or less; and (3) the relief of symptoms brought about by the administration of glucose. Blood sugar above 50 mgm. per 100 cc. during an attack points to other causes than islet adenoma. The etiological factors may be found in Table I.

Also under these circumstances a diet low in carbohydrate (50 gm. or less) and high in protein often gives relief from attacks. This is due to the fact that while 50 per cent of the protein may yield dextrose the slow even rate of conversion, as well as the slower absorption rate of protein, prevent marked elevation of the blood sugar which would in turn stimulate the pancreas. The glucose tolerance curve is influenced by the antecedent diet in normal people as well as in those with hypoglycemia. A glucose tolerance test taken after a proper preparatory diet has definite diagnostic value in hypoglycemia. Both organic and functional hyperinsulinisms characteristically give a low dextrose tolerance curve, and the organic type usually has an abnormally low fasting level. In borderline cases studies on the utilization of injected glucose are indicated. The authors take the basal metabolic rate prior to the injection of glucose, and repeat this test at one-half hour, one hour, two and one-half hours and three hours after the injection. Urine examinations are made for nitrogen and sugar if the proportion of carbohydrate, fat, and protein utilized is to be determined. The calculation of the respiratory quotient gives diagnostic information and is of benefit also in following the patients postoperatively. In patients not conforming to the "Whipple triad" and yet presenting the symptoms of hyperinsulinism these studies may aid in determining the advisability of performing a subtotal pancreatectomy.

Two cases are presented which were characterized by the syndrome of spontaneous hypoglycemia, and the fact that no islet tumor could be found. The results obtained following subtotal resection of the pancreas in these cases were very satisfactory. The study of the metabolism of glucose in these patients after

TABLE I—ETIOLOGICAL CLASSIFICATION OF SPONTANEOUS HYPOGLYCEMIA (CONN)

- I Organic—recognizable anatomic lesion
 - (a) Hyperinsulinism
 1. Pancreatic islet cell carcinoma
 2. Pancreatic islet-cell adenoma
 3. Generalized hypertrophy and hyperplasia of the islets of Langerhans
 - (b) Hepatic disease
 1. Ascending infections—cholangitis
 2. Toxic hepatitis
 3. Diffuse carcinomatosis
 4. Fatty degeneration or metamorphosis
 5. Glycogenosis (von Gierke's disease)
 - (c) Pituitary hypofunction (anterior lobe)
 1. Destructive lesions (chromophilic tumors, cysts, etc.)
 2. Atrophy and degeneration (Simonds' disease)
 3. Thyroid hypofunction—secondary to pituitary hypofunction
 - (d) Adrenal hypofunction (cortex)
 1. Atrophy or destruction of cortex
 - (e) Lesions of the central nervous system (some interfere with nervous control of the blood sugar)
- II Functional—no recognized anatomic lesion
 - (a) Hyperinsulinism (imbalance of the autonomic nervous system)
 - (b) Renal glycosuria
 - (c) Pregnancy and lactation

they had been on a standard preparatory diet, was of benefit in a diagnostic way and also in evaluating the results of treatment. The authors have indicated the results of the preoperative and postoperative glucose tolerance tests and the phosphorus curves in both of their patients by a series of charts. One of the cases required very extensive pre- and postoperative studies.

The first patient was a white, single, female, nineteen years of age. On April 11, 1935 her complaints were severe headache, abdominal cramps, chronic cough and an excessive gain in weight. Roentgenograms of the chest and skull were negative. The basal metabolic rate was -5. The patient was taking 1 gr. of thyroid daily. The fasting blood sugars were 78 and 99 mgm. per cent.

In January 1936 frequent attacks of weakness, sweating, tremor and a stuporous mental reaction were noted. Lack of food induced these conditions, and ingestion of carbohydrates brought quick relief. The blood sugar levels taken during the attacks were from 35 to 60 mgm. The usual routine laboratory examinations were negative. The clinical diagnosis was spontaneous hypoglycemia. At operation approximately two-thirds of the pancreas was removed. During the operation the patient was given 400 cc. of glucose and 500 cc. of whole blood intravenously. Postoperative blood-sugar determinations were made hourly and measured 250, 230, 230, 170 and 140 mgm. per cent, respectively. Fasting

blood-sugar determinations were made daily and measured 135, 129, 111, 129, 105, 91, 75, 93, 96, 84, and 89 respectively. The postoperative course was uneventful; the patient remained asymptomatic, blood-sugar tests taken each year have remained normal.

The gland tissue excised was normal.

The second case presents a more complicated picture. The patient was white, female, age forty-three. The first complaints were of nervousness, backache, low blood pressure, and sinus trouble. The first attacks of nervousness in 1929 were characterized by weakness, irritability, excessive perspiration, and ravenous hunger all occurring about three hours after meals and being worse after exercise; they were relieved by eating, especially readily available carbohydrates. There was a gradual loss in weight. The attacks became progressively more severe and further symptomatology included memory loss during the attacks, mental cloudiness, speech difficulty and visual disturbances but no loss of consciousness. Physical examination was essentially normal. The usual laboratory tests were negative. The fasting blood sugars varied from 61 to 69 mgm. per cent. Roentgenograms of the spine, skull, chest, gall bladder, stomach and duodenum were normal. Severe symptoms were induced in the fasting state by strenuous exertion at which time the blood sugar measured 60 mgm. per cent. One milligram of epinephrine was given subcutaneously with relief of all the symptoms within fifteen minutes, when another blood-sugar specimen measured 73 mgm. per cent.

The patient at this time was discharged on a high protein, low carbohydrate diet, with 5 to 6 meals daily and thyroid extract (1/4 gr.) daily. Symptoms became gradually more severe and the patient was again admitted to the hospital on two different occasions about three months apart. Glucose-tolerance tests were again made on each of these occasions, and the last one had to be terminated at the end of one and three-fourths hours because of the severity of the hypoglycemic reaction. Further laboratory tests were made. The blood nonprotein nitrogen measured 26.5 mgm. per cent, the blood sodium 33; the blood potassium 17.5. The basal metabolism rate was now +4, and the respiratory quotient 0.80.

The patient was given 500 cc. of 10 per cent glucose intravenously in preparation for the operation. In one and one-half hours a reaction occurred which required the injection of 50 cc. of 50 per cent glucose for relief. During the operation 500 cc. of 10 per cent glucose and 500 cc. of whole blood were given intravenously. Approximately five-sixths of the pancreas was resected, but no adenoma was found. Postoperative blood-sugar determinations were made hourly and measured 108, 91, 85, 109, 127, 131, 145, 112, 132 and 98, respectively. The daily blood sugar varied between 80 and 100 mgm. per cent. The postoperative course was completely uneventful with the patient returning to excellent health. The fasting blood-sugar level has been between 80 and 90 mgm. per cent since the operation.

In both cases the microscopic appearance of the pancreas was normal and no islet adenoma was found. The excellent results following subtotal pancreatectomy have led the authors to recommend this as a procedure of choice when no adenoma can be found after a careful search of the pancreas and the usual sites where heterotopic pancreatic tissue sometimes occurs. A large amount of pancreas must be resected in these cases. The function which the pancreas plays in the digestion was not affected significantly when four-fifths of the gland had been removed. Neither were there any metabolic disturbances.

The authors prescribe a high protein, low carbohydrate diet for preoperative trial. They have experienced difficulty in getting patients to refrain from the ingestion of some carbohydrate when the unpleasant prodromal symptoms appeared. The patients' complete confidence is necessary to keep them from escaping this by taking a little carbohydrate, which they have found relieves them, at least temporarily.

The authors point out that hyperplasia of the islet cells is difficult to be sure of pathologically, just as it is difficult to tell which tumors are benign and which are malignant. Especially is this true since the microscopic appearance of the gland in both cases reported was described as normal.

MATTHEW J. SINGER, M.D.

MISCELLANEOUS

Senger, F. L., and Bottone, J. J.: Perirenal Insufflation. *Am. J. Surg.* 1944, 66: 3.

Perirenal insufflation has proved to be of great value in the differential diagnosis of all retroperitoneal lesions in and about the kidney. Its use permits conclusions concerning the local spread and operability of renal tumors. The technique is not difficult, and can be mastered easily. Complications are infrequent, and are of only minor degree, if ordinary care is taken.

A series of 175 consecutive cases in which perirenal insufflation was done is presented; no serious mishap occurred. In all instances added valuable information was obtained. The method should be employed in all indicated cases, although its indiscriminate use is discouraged. No elaborate or expensive equipment is necessary.

SAMUEL KARY, M.D.

Gisgett, O. T., and Tinney, W. S.: Subphrenic Abscess, with Special Reference to Intrathoracic Complications. *Am. J. Surg.* 1944, 66: 89.

Subphrenic abscess can occur after any abdominal operation or any inflammatory process in the abdomen. Too often it is not recognized until serious thoracic complications have developed. Thoracic complications, which are late complications of subphrenic abscess, are responsible for the high mortality rate of this condition. Early recognition and treatment of subphrenic abscess will prevent thoracic complications.

The diagnosis is not difficult in most instances. A history of an abdominal condition which could cause a subphrenic abscess, with evidence of a suppurative process manifested by fever and elevation of the leucocyte count, which cannot be accounted for otherwise, is sufficient to warrant investigation. Anteroposterior and lateral roentgenographic views of the diaphragm with the patient in the erect position are of greatest value. The presence of a fluid level under the diaphragm was demonstrated in this manner in about 25 per cent of the authors' cases. Marked elevation and immobility of the diaphragm are significant. It is generally agreed that diagnostic aspiration should never be attempted in cases of suspected subphrenic abscess. The subphrenic region is not anatomically suited to such procedures as it is necessary to traverse either the peritoneal or pleural cavities with the needle in such cases and the danger of setting up infection in these cavities is very great. Furthermore failure to obtain fluid proves nothing. Exploratory operation is without question the logical and safe procedure in cases of suspected subphrenic abscess.

The extracorporeal approach to subphrenic abscesses is the safest and most effective means of treating them.

The approach to abscesses situated anteriorly as indicated by the lateral roentgenogram is made by an incision just below the costal arch. The incision is carried down through the muscle and posterior fascia to the peritoneum. A line of cleavage is estab-

lished just outside of the peritoneum and by blunt dissection the peritoneum is stripped from the under surface of the diaphragm until the induration and fluctuation of the abscess are demonstrated. An opening is then made into the abscess sufficiently large to establish adequate drainage.

For abscesses situated posteriorly it is necessary to resect the twelfth rib. Meinkoff has demonstrated that in about 62 per cent of cases the pleura extends to the twelfth rib but it never extends as low as the spine of the first lumbar vertebra; therefore a transverse incision is made across the posterior bed of the twelfth rib at the level of the first lumbar spine and, by blunt dissection, a line of cleavage is established below the diaphragm but outside of the fascia enclosing the kidney and adrenal glands, and the dissection is extended until the abscess is reached.

These approaches can be carried out quickly and easily even on patients who are extremely ill. After the establishment of adequate external drainage of these subphrenic abscesses rapid improvement takes place, and in cases complicated by bronchial fistula the fistula closes and the cough clears up rather rapidly. If the bronchial fistula has been present for some time before drainage of the subphrenic abscess is established bronchiectasis may develop in the lung from chronic inflammatory changes in the bronchi, even though the abscess heals satisfactorily. This fact indicates further the importance of early diagnosis and drainage of subphrenic abscess.

GYNECOLOGY

UTERUS

Tribedi, B. P., and Da, S. N.: Observations on Chronic Endometritis. *J. Ind. M. Ass.*, 1944, 13, 30

Two hundred and twenty three pathological specimens were studied with regard to the incidence of chronic endometritis. These were from records accumulated over twenty years in the Pathology Department of the Calcutta Medical College. The study was undertaken because chronic endometritis has been a subject causing considerable confusion.

According to the modern conception, chronic endometritis has the following three characteristic features: (1) it is a rare if not altogether impossible, affection of the endometrium, as the latter does not lend itself to any chronic inflammation because of the simple tubular character of its glands and the regular monthly shedding of its superficial layers in the nonpregnant fertile stage of life; (2) it must be associated with some adjacent nidus of infection in order that the chronic inflammatory condition in the endometrium may be maintained for a prolonged period; and (3) it must exhibit histologically a large number of plasma cells. The presence of these cells in number will differentiate chronic endometritis from an otherwise normal endometrium in the premenstrual stage in which round cells together with glandular hyperplasia, hypertrophy and irregularity, misled Ruge to coin the name "glandular endometritis."

The author then presents his observations from the study of these records and attempts to assess how far this survey fits in with the current conception of chronic endometritis. The various pathological pictures described in these records are classified into eight groups, presented in a tabulated form in order to see how far they satisfy the criteria laid down for the acceptance of the condition described as chronic endometritis. The author discusses in detail the findings in these various categories of classification.

By observing closely for the three characteristic features as required by the modern conception of the subject, particularly the presence of large numbers of plasma cells, only 1 case of true chronic endometritis among the 223 cases was found. The rest of the cases would appear to be doubtful.

The author discusses the significance of the presence and absence of plasma cells in the various pathological conditions of the endometrium. In certain of these conditions, as, for example, in tuberculous of the endometrium, the plasma cells are not detected and the presence of lymphoid cells is depended upon mainly for the diagnosis. In conclusion, the author states that less confusion will result if the 3 characteristic points relative to the modern conception of endometritis are remembered.

HARRIET F. THURGOOD, M.D.

Barrett, C. W.: The Place of Surgery in Fibroids of the Uterus. *Am. J. Surg.* 1944, 66, 148.

The author discusses the history and the current treatment of fibroid tumors of the uterus. He outlines the indications and contraindications for various methods of dealing with the tumors and concludes that they should be treated by one of the following methods:

1. Observation for small asymptomatic tumors.
2. Surgery for larger symptom-producing tumors, particularly in young women in whom the genital functions can be preserved for large tumors at the menopause or for tumors in the postmenopausal patient in which evidence of activity is found.
3. Radiation castration for small tumors at the menopause when the only symptom is bleeding and when there is no contraindication to radiation.

J. ROSSAR WILLSON, M.D.

TeLinde R. W., and Galvin, G.: The Minimal Histological Changes in Biopsies to Justify a Diagnosis of Cervical Cancer. *Am. J. Obs.* 1944, 45, 774.

From a study of the material from 11 cases, the authors have concluded that the abnormal cellular activity which eventually results in fully developed cancer begins in the basal cells of the surface epithelium. In the normal cervical epithelium there is a single layer of fat spindle cells forming the basal layer. They stain deeply with hematoxylin. The transition from this normal picture to extreme basal-cell hyperactivity involving the full thickness of the surface epithelium may be shown histologically in a variety of ways. The normal and hyperactive epithelium may be demarcated by the often-described short oblique line of Schiller. The authors have observed more often however a gradual transition from slight overactivity to a complete involvement of the full thickness of the epithelium by hyperactive epithelial cells. On the other hand, they have rarely observed an absolutely abrupt change. Regardless of the manner of transition, when the full thickness of the epithelium is made up of this hyperactive basal epithelium, the ultimate picture is the same. There is a complete loss of the normal stratification of the cells, the cells and especially the nuclei are irregular in size and shape and a variable number of mitotic figures are present.

After the hyperactive basal epithelium, the next step is invasion of the subepithelial tissue. The glands seem to afford a favorite route for invasion of the underlying tissue. The columnar epithelium lining the gland is destroyed as the epithelium advances. When the base of the gland is reached, the malignant epithelium continues its growth into the depth of the tissue. There is a distinct difference between this process and that seen when the columnar lining of a gland is replaced by the benign

process of epidermization. Aside from the difference in character of the individual cells taking part in invading the gland there is the difference that when the lumen of the gland is filled in its length and breadth by the epidermization process the growth ceases, whereas the malignant growth continues into the adjacent tissue.

There is the strong suggestion that all epidermoid cervical cancer arises in the basal-cell layer regardless of what cell type predominates ultimately in the fully developed cancer.

The astonishing thing in making this study was the frequency with which these lesions occurred in the authors' laboratory. Eight of the 11 cases were found within a twelve month period. During the time, 704 cervical biopsies were made. This incidence was much greater than any that had ever occurred in the laboratory during any corresponding period of time. Certainly it behooves the gynecologist who performs subtotal hysterectomy frequently to perform biopsy freely of all cervixes on the slightest suspicion. EDWARD L. CORNELL, M.D.

Melno, C. B., Broders, A. C. and Munsey, R. D.: Pathology of Malignant Neoplasm of the Cervix Coincident With Pregnancy. *A. J. Obs.* 1944 48 806

A study of 3,570 cases of carcinoma of the cervix observed at the Mayo Clinic in approximately thirty-two years revealed that pregnancy was present in 26 or 0.7 per cent, of these cases when the carcinoma was found. This figure does not necessarily indicate the true incidence of carcinoma of the cervix coincident with pregnancy as all of the 3,570 patients came to the clinic because of carcinoma of the cervix and not because of pregnancy. In the same period covered by this study 8,500 pregnant women were observed at the clinic.

The average age of the patients in the 26 cases in which carcinoma of the cervix was coincident with pregnancy was thirty-two years. The youngest patient was twenty-five years of age and the oldest was forty-one years of age. The prognosis was no worse in the young patients than it was in the older ones.

The average number of previous pregnancies was 6 and the average number of children was 4. The number of pregnancies apparently did not affect the prognosis. In cases in which the carcinoma was diagnosed in the later months of pregnancy the lesion usually was well advanced and the prognosis was poor.

Pregnancy may occur after carcinoma of the cervix has developed. A family history of carcinoma was elicited in 7 or 35 per cent, of the 20 cases which were observed five or more years prior to 1941. The prognosis in these 7 cases was better than the prognosis in the remainder.

Bleeding was the initial symptom in 23 or 88.5 per cent, of the cases. In 25 per cent, the patients did not realize that they were pregnant when the diagnosis was made.

No definite conclusions can be drawn concerning the relative value of irradiation therapy; however, it appears that operation is preferable in cases in which the lesion is operable and that supplementary irradiation increases the percentage of good results. This is in contrast to the relative value of irradiation therapy and hysterectomy in cases of carcinoma of the cervix in which the patients are not pregnant.

The authors are in general agreement with Strauss concerning the treatment of carcinoma of the cervix coincident with pregnancy. If the extent of the lesion permits operation and if the fetus is not yet viable, total hysterectomy is followed by irradiation. If the lesion is operable and the fetus is viable, cesarean section is followed by panhysterectomy and postoperative irradiation.

In cases in which the lesion is nonoperable and the fetus is viable, cesarean section is followed by irradiation. In cases in which the lesion is nonoperable and the fetus is not yet viable, sufficient irradiation is employed to treat the lesion; abortion occurs.

In cases in which the lesion is operable, total abdominal hysterectomy has produced the best results. In 57 per cent of the cases in which this procedure was employed, the patients were free of recurrence five years after the operation.

In this series of cases of carcinoma of the cervix coincident with pregnancy, many of which were observed before the present methods of treatment were developed, the prognosis appeared to be at least as favorable as the prognosis of carcinoma of the cervix that is not associated with pregnancy. Of the 20 patients who were followed up, 30 per cent were free of recurrence five or more years after they had been treated at the clinic.

Schlink, H. H., and Chapman, C. L.: Cancer of the Cervix Uteri, 1930-1942. *Med. J. Australia* 1944 1 377

In 1929 the three clinical schools of Sydney agreed to adopt different forms of treatment for cancer of the cervix uteri and then meet every five years to compare results. The Royal Prince Alfred Hospital was allotted the task of recording the results from the use of radium combined with surgery. Chapman and Schlink have kept faithfully to the plan arranged but for some reason or other there have never been the five-year scheduled comparisons with the other groups.

Ten years have elapsed since these two authors started to record their results in detail and they believe their presentation to be of interest to cancer workers not only in Australia but wherever interest is taken in the subject.

In the past they believe overenthusiastic advocates of particular methods of treatment have prevented the real truth from being discovered. Furthermore, they are strongly of the opinion that relative statistics have led to confusion and that nothing but absolute statistics should be accepted as the standard for comparing figures presented by the various clinics of the world.

TABLE I—RESULTS OF TREATMENT

Condition of Patients	Five Year Statistics, Royal Prince Alfred Hospital 1920-1925		Aggregate Figures from Sixteen World Centers (Bourne and Williams)	
	Cases	Per cent	Cases	Per cent
Patients seen with view to treatment	28		2,051	
Patients treated: 10 cancers microscopically proved	46	5.1	7,052	87.8
16 local recurrence after five years	7	30	2,194	27.6
Dead of cancer	34	6.6	5,768	67.5
16 with recurrence at or in five years	3		18	4
Dead of operation (subjected to operation)		1.5		
Dead of radium treatment (54 cases)				
Dead of recurrent disease		6		
Lost				3
Five-year cure percentage among all patients seen		18.6		
5 cur survival rate among all patients seen		29.4		1.6

Attention is directed to Bourne and Williams who have published in their fifth edition of "Recent Advances in Obstetrics and Gynecology" a clear analysis of often conflicting results in the treatment of cancer of the cervix uteri by radiotherapy. The summarized figures from sixteen world centers are here available so as to be understandable even to the busiest general practitioner.

The method of treatment used by these authors has been to give all the patients treated one full dose of radium, from 5,000 to 7,000 mgm.-hr. with 1 mm. of platinum screenage to the uterus and 2 mm. of platinum screenage to the vagina, and after five weeks those considered operable were submitted to Wertheim's radical hysterectomy.

The above table shows that the use of surgery in addition to radium saves an extra 4.4 per cent of all patients examined over those treated by radiotherapy alone.

The 246 patients treated, 84 of whom have qualified for the ten year statistics, show that the cure rate of radium treatment and surgery fell from 56.1 to 55.1 per cent in contrast to the cure rate of radium treatments which fell from 8.1 to 4 per cent. This would indicate that among the five-year cures 50 per cent of the patients treated by radium alone will perish before they reach their tenth year from the commencement of treatment.

In order to discover the best form of treatment for this lethal disease, it would be far better for all workers to discard all those patients who are suitable for palliative treatment only and concentrate on those who may be salvaged. Certainly with the

forms of treatment at our disposal no real advancement in cure can be made unless the patients are seen in the first and second stages. When the fourth stage is excluded in the authors' statistics the results are most enlightening. There were 16 patients in stage 1 treated by combined radium and surgery. At the end of five years 13 or 80 per cent, were alive there were 53 patients in stage 2 and 60 per cent were alive at the end of five years and there were 43 in stage 3 of which 18 or 41 per cent, were alive at the end of five years. This made a total of 112 patients of whom 63 or 56.1 per cent, were alive at the end of five years.

In the 212 cases treated by radium followed by Wertheim's hysterectomy the operative mortality was 3.5 per cent. The operation itself has the advantage of removing invaded lymphatic glands. In the authors' material, 30 per cent of the cases presented carcinomatous glands. Since the majority of radiotherapists admit that treatment by radium or x ray has no effect on cancer in the lymph glands, it is reasonable to suppose that the authors' better results obtained by combined radium therapy and surgery were due to some degree to the fact that 30 per cent of the invaded material was removed by operation.

SAMUEL J. FOX, M.D.

ADNEXAL AND PERIUTERINE CONDITIONS

Karnaky, K. J.: A New Treatment for Microcystic Ovaries by the Use of Diethylstilbestrol. A Five Year Study. *West J Surg* 94:4, 5:597

The author notes that the question of what to do with the small cystic ovary or ovaries, occurring with or without pain and of less than 5 cm. in diameter has been a problem of the medical profession since the day of Ephraim McDowell. There are still many useful ovaries in young and old women being sent to pathological laboratories because the surgeon on pelvic examination or at operation has regarded them as "microcystic ovaries."

The endocrine control of the ovary is discussed in some detail. The most common cysts of the ovaries and the ones so easily treated by diethylstilbestrol are (1) follicular cysts that originate in graafian follicles by cystic change. These are in reality retention cysts rather than new growths or proliferative processes. These cysts may be due to a thickening of the epithelial covering of the ovary as a result of inflammation, which prevents rupture of the follicles. (2) There is also microcystic or polycystic degeneration of the ovaries which appears as congeries of numerous, tense, thick or thin walled follicles of pea to cherry size, projects above the surface, and gives the enlarged ovary a bossed appearance.

The ovaries are often riddled by retention follicular cysts, which often causes enlargement, pressure, and a fluctuation in the estrogenic blood level. There may be pelvic pain and menorrhagia. With the exception of incomplete abortion, retention cysts of the ovary are the most common cause of abnormal uterine bleeding. In normal menstruation the

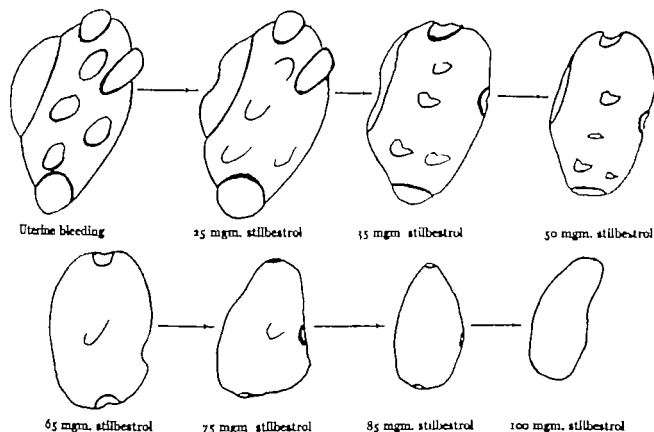


Fig. 2. Effect of diethylstilbestrol on small follicular cyst of the ovaries. Diethylstilbestrol causes complete but

temporary atrophy of the ovaries. Diethylstilbestrol can be used for the treatment of microcystic ovaries.

follicular cyst ruptures which throws the ovum into the pelvic cavity or into the fimbriated end of the tube. If the ovum does not rupture then abnormal menstruation occurs.

The action of diethylstilbestrol in favorably affecting abnormal uterine bleeding is based on the fact that it causes temporary atrophy of follicular cysts of the ovary. Under stilbestrol therapy small unilateral or bilateral cysts up to the size of a small lemon will generally regress to a size that cannot be felt by pelvic examination.

A classification of ovarian cysts is presented by the author. The details of the administration of stilbestrol to a group of patients with cystic ovaries are given.

Diethylstilbestrol which causes a temporary atrophy and complete obliteration of the follicular cysts of the ovaries, can be used to evaluate the condition of the ovary, hence the author notes that we can tell without opening the abdomen whether or not the ovary should be removed in approximately 98 per cent of the cases.

If the patient is given 5.0 mgm of diethylstilbestrol every night for thirty or more nights and the ovarian cyst or cysts still persist then one can feel that he has a very good indication for subjecting his patient to a laparotomy. Normal ovaries will undergo atrophy while abnormal ovaries will not hence diethylstilbestrol used preoperatively will save many needless operations because if the ovary is atrophic

and free of follicular cysts, then that ovary may be left in and the operator may feel that he has not left in an abnormal ovary. On the other hand, if the ovary or ovaries have not become atrophic and devoid of follicular cysts the operator will have a good criterion as to which ovary or ovaries to remove. This would save many normal ovaries that are now going to the pathological laboratories.

If one feels an enlarged ovary from 3 to 5 cm in diameter and if it does not get smaller after giving 5.0 mgm. of diethylstilbestrol every night for twenty or more nights, then an operation is in order. If the ovary is about 3 cm. in diameter then 3.0 mgm of diethylstilbestrol can be given every night for forty nights.

HENRY F. THURSTON, M.D.

EXTERNAL GENITALIA

Ayre, J. E.: Cyclic Ovarian Changes in Artificial Vaginal Mucosa. *Am. J. Obst.* 1944 48 690.

A case of congenital absence of the uterus, vagina and hymen is presented with a simple method of producing a satisfactory artificial vagina without resort to major surgery. The patient was kept ambulatory.

The patient was hospitalized and under anesthesia an opening was made between the bladder and the rectum to admit one finger. No further penetration was attempted at this time because of the extremely thin membrane between the rectum and bladder. The new passage was devoid of any epithelial lining.

and in an effort to keep it open a wax mold (dental wax) was inserted this was lubricated with sulfa thiazole paste.

The patient was allowed to leave the hospital in a few days the obturator being held in place comfortably by a common menstrual belt and pad. She was seen each week when the mold was removed, the cavity cleaned out and the marginal rim of the vulval mucous membrane was cauterized with 30 per cent silver nitrate. On each visit it was observed that the squamous epithelial zone had crept a little higher up the canal to form a sleeve around the obturator until finally the entire canal was covered.

Cyclic ovarian changes have been demonstrated in the artificial vaginal mucosa with differentiation of the two phases (follicular and luteal) in the vaginal smears. A cornification curve representing the variable quantitative level of estrin secretion would appear to follow the approximate anticipated pattern in accord with the cyclic phases. The approximate times of ovulation and menstruation have been hypothesized. **LEONARD L. CORNELL, M.D.**

MISCELLANEOUS

Widenius, I. E.: A Study of Commercially Manufactured Catamenial Tampons. *Am J Obst Gyn*, 48: 30.

A study of 6 commercially manufactured tampons used for the control of the menstrual flow in women was conducted on a group of 25 women of varying ages and pelvic types. Five of the 25 women subsequently desired childbearing and succeeded therefore the use of tampons does not prevent conception. Nine of the 25 women had used tampons at some time previous to this study which indicated a fairly widespread acquaintance with the use of tampons as a method of controlling the catamenial flow.

Description of the amount of flow by a patient is not always consistent with the number of pads used, which indicates that adequate protection can be judged only by correlating the length of complete protection with the definite amount of menstrual flow which can be determined only by weight.

Seven of the 25 women had cervical erosions, but only 2 of the 7 had used tampons previously. Of the 2 who had used tampons previously one had a lacerated cervix resulting from childbirth and the other had an erosion which is commonly classified as a congenital erosion of the cervix.

Four of the 6 tampons were inserted manually by the women and 2 were inserted by the use of individual inserters. The use of an inserter permits proper placement of the tampon within the vaginal tract without contamination by the fingers. Three of the 6 tampons were of the nonexpanding type with a fixed length. Tampon No. 1 was the shortest, being only 1 3/4 inches. Tampons No. 3 and No. 4 were both over 2 inches in length. Clinical findings favor the shorter tampon.

The remaining 3 tampons were of the expanding type. Tampon No. 2 had a fixed length of 2 3/4 inches and expanded only laterally. The 2 others expanded both laterally and lengthwise. Tampon No. 7 had a fixed length of 4 inches before compression and the other tampon, No. 12 had a fixed length of 2 inches before compression.

Roentgenogram visualization of the position in action of catamenial tampons indicates that tampons approximately 2 inches in length are least likely to detect the cervix in the average woman. Tampons with a rounded base are readily removed.

The study taken as a whole leads to the conclusion that catamenial tampons can be used by the average woman to control an average catamenial flow with safety, comfort and complete protection, provided that a short tampon is properly placed well into the introitus. **EDWARD L. CORNELL, M.D.**

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Hill, J. H. and Trimble, W. K.: Placental Infarction as a Diagnostic Criterion of Maternal Toxemia. *Am. J. Obst.* 1944 48 632.

The placentas from 640 consecutive deliveries were fixed in 10 per cent formaldehyde solution for from four to six weeks and then examined grossly for certain infarcts involving necrosis of the villi. Forty-two placentas were from patients with a definite clinical picture of toxemia.

Upon examination only 8 of these 42 placentas from cases of toxemia had such infarcts which were extensive enough so that they could be distinguished from placentas of nontoxemia cases. Thirteen of the 593 placentas from patients with normal pregnancies showed infarcts like the 8 from the cases of toxemia.

The authors were unable to satisfy themselves that they could definitely state that the acute type of infarct described by Bartholomew and his co-workers was associated with toxemia.

In 25 placentas, the cord was drained. There were no instances of congestion when this was done. The administration of pituitrin at the end of the second stage of labor did not affect the incidence of congestion. Congestion might obscure some placental infarcts.

EDWARD L. CORNELL, M.D.

LABOR AND ITS COMPLICATIONS

Persall, J. T., and Torpin, R.: Placenta Previa: Report of 170 Cases. *J. M. Ass. Georgia*, 1944, 33: 297

This is a study of a series of 170 cases of placenta previa observed in the University Hospital in Augusta, Georgia and extends over rather a long period about twenty years. All cases were treated by many physicians and various members of the staff.

The most valuable contribution of the paper is that it shows the relative racial frequency of placenta previa among negroes and whites. The racial proportion of the population in the vicinity of Augusta, Georgia is 58 per cent white and 42 per cent negro and the authors think that this study shows that placenta previa is more common in the white race than in the colored race—in about the ratio of 64 to 36. It would also seem to indicate that the condition is relatively rare in primiparous negroes. Among the 170 cases of placenta previa 15 deaths occurred a total mortality of 8.5 per cent. Hemorrhage was the principal factor in 10 of these deaths, and infection in 5. It should be stated that 4 cases reached the hospital moribund and death could not be avoided by the obstetricians.

Only 21 per cent of all cases received a transfusion which is a very low figure compared with the present trend, but when one considers that these statistics were compiled over a period of twenty

years it is probably a fairly good percentage when put on a comparative basis with other institutions over the same period of time. As the authors state the lesson to be learned from this high mortality record is that every woman should be within range of a blood bank with at least 4 pints of blood of each type available at all times, and that women should be taught the danger of third trimester hemorrhage.

The authors' method of choice for treating this condition is apparently cesarean section, but in certain cases in which the patient is multiparous and the condition is favorable, a Voorhees bag should be used and followed by version if bleeding again occurs as the bag comes out. CHARLES E. GALLOWAY, M.D.

NEWBORN

Sandifer, S. C.: Premature Birth (Analysis of 1 000 Cases) Incidence Etiology and Immediate Result to the Baby. *J. Obst. Gyn. Brit. Empire* 1944 51 408.

The Statistical Review of the Registrar General for England and Wales disclosed that in 1938 there were 24,729 stillbirths 17 572 neonatal deaths and 621 204 live births. Roughly half of the stillbirths and neonatal deaths were associated with prematurity which gave a combined death rate associated with prematurity of 33.1 per 1,000 total births.

An analysis of 1,000 cases of premature birth was made to determine the causative factors. The incidence of premature labor at Queen Charlotte's Maternity Hospital was 8.11 per cent. In the registered group it was 6.78 per cent and in the emergency group 17.2 per cent. One hundred and ninety premature labors were induced in the registered group of 781 which yielded a corrected premature birth rate of 5.13 per cent.

No cause for premature birth was found in 372 (37.2 per cent) of the cases. Induction accounted for it in 319 (31.9 per cent) and abnormalities of the mother and fetus were the causes in the remaining 309 (30.9 per cent). The indications for induction and the abnormalities associated with spontaneous premature labor are shown in two charts.

The stillbirth rate in this group was 25.2 per cent the neonatal death rate was 14.4 per cent and the total death rate 39.6 per cent. With regard to fetal size these statistics revealed the usually expected mortality rates.

The author believes that obstetric pathology was associated with the majority of the premature labors. Medical complications were no more frequent in the premature children than in the mature. Prenatal care adequate diet, and sufficient rest in the latter part of pregnancy should reduce the incidence of the most common causative factors such as toxemia, multiple birth and antepartum hemorrhage.

JAMES F. DONNELLY, M.D.

Lubinski, H., Benjamin, B. and Stream, G. J.: Observations on the Rh Factor in Its Relation to Hemolytic Anemia of the Newborn Infant. *Am. J. Obst.* 1944, 48: 464.

In six families there occurred 6 cases of hemolytic anemia of the newborn, and there was evidence that 7 other infants had probably suffered from this disease.

Common to all of the cases tested was the combination of the following conditions: the mother was Rh-negative, the father was Rh-positive (only one father was not available for testing) and the infant was Rh-positive. All the mothers had anti-Rh agglutinins in their sera.

Immunization of an Rh-negative woman by repeated transfusions of presumably Rh-positive blood was later followed by fatal hemolytic anemia of her first newborn infant. Rh-negative females should not be transfused with Rh-positive blood to prevent the possibility of this undesirable effect upon any future Rh-positive offspring.

A possible role of complement and of the liberation of hemolysins after the destruction of red blood cells in the clinical picture of hemolytic anemia of the newborn is discussed.

No correlation was found between the titer of anti-Rh agglutinins in the mother's serum at parturition and the severity of hemolytic anemia in her newborn infant.

As the treatment of choice for this disease, the infant should be given a transfusion of a concentrated suspension of washed Rh-negative red blood cells as early as possible and this should be repeated as often as may be necessary. A suspension of washed cells from the mother's blood may be used if no suitable donor is available. Washed cells from the mother's blood should be used in any case in which the mother and her newborn infant who shows evidence of the disease are both Rh-positive or both Rh-negative. EDWARD L. CONNELL, M.D.

Starrock, J.: Obstetrical Responsibility in the Prevention of Fetal and Neonatal Deaths. *Edinburgh M. J.* 1944, 5: 147.

The stillbirth and infant mortality rates in Scotland are high. In Scotland in 1939 there were 108 deaths per 1,000 total births, 43 were stillbirths, 35 were neonatal deaths (deaths before one month of age) and 31 were deaths occurring between the end of the first month and the end of the first year. This compares unfavorably with New Zealand, Holland, Canada, England, and Wales. In Scotland over 70 per cent of these fatalities are due to stillbirths and neonatal deaths. In view of the records for the next eleven months the authors believe that control of postnatal infection—especially pneumonia and gastroenteritis—is the secret of successful reduction of these deaths.

The problem of how to diminish the number of stillbirths and neonatal deaths is primarily an obstetrical responsibility as an examination of their causes makes obvious.

We have no knowledge of how to prevent congenital defects but there is a considerable accumulation of information regarding the control of prematurity, asphyxia, and intracranial hemorrhage. An appreciation of these causes of death and the factors that produce them and the faithful application in daily practice of methods that control them are the contributions which obstetricians, family doctors, and midwives can make.

Prematurity, now defined as a viable child weighing 5½ lb. or less at birth is of great importance. Prematurity was a factor in 436 about 50 per cent, of 813 stillbirths and neonatal deaths although it was considered to be the primary cause of death in only 43 cases. Immature children are more vulnerable to the other lethal factors of asphyxia, cerebral hemorrhage, and infection than full-term children.

In 66 per cent of the fully investigated cases of death among premature infants in the Maternity Pavilion there was an associated abnormal pregnancy. The main complications were antepartum hemorrhage in half (48 per cent) of these abnormal pregnancies and preclampsic toxemia and eclampsia in a fifth of them while hydramnios, pyelitis, and cardiac disease were less frequent factors. In the remaining third of these premature cases the pregnancy had been normal until the onset of labor but no satisfactory explanation of the early onset of labor could be found.

Can anything be done to prolong these gestations? Recent experiments and observations have shown that the correction of dietetic deficiencies appears to play a part in reducing the incidence of premature labors and helps to control the development of the more serious manifestations of toxemia, so that the necessity for termination of pregnancy can be delayed. Accidental hemorrhage is often linked up with pre-eclampsic toxemia and hypertension and, in the absence of these, the possibility of a vitamin C deficiency has been suggested as an etiological factor. Education in the matter of diet is one practical step we can take in our antenatal clinics and private practice. In addition to diet, the provision of proper rest and house help for pregnant women would also be beneficial.

Asphyxia was the actual cause of death in 40 per cent of the stillbirths and 30 per cent of the neonatal deaths. It is produced in at least four common ways: premature separation of the placenta, obliteration of the cord circulation, prolonged labor and the development of anoxemia from overdosage of the mother with analgesic drugs or during general anesthesia when cyanosis is allowed to occur. Premature inspiration is probably more commonly the result of developing asphyxia and of course aggravates it.

Premature separation of the placenta, frequently complicated by immaturity of the fetus, accounts for a high proportion of fetal deaths due to asphyxia. In the cases seen from 1940 to 1943 in the Simpson Maternity Pavilion it occurred in 129, or 45 per cent, of the 285 fatalities confirmed by postmortem examination as primarily due to asphyxia. Our present

state of knowledge does not permit of our taking steps to prevent placenta previa or accidental hemorrhage with the possible exception of counteracting the factor of malnutrition which accounts for some cases of accidental hemorrhage. Therefore these fetal deaths must largely be considered non preventable. It should be remembered however, that avoidance of overtreatment in minor degrees of placenta previa and recourse to cesarean section in the major degrees especially if the child is near term not only preserves some fetal lives but is usually safer for the mother.

Fetal asphyxia due to the other causes, obliteration of the cord circulation prolonged labor and anoxemia during anesthesia, is for the most part theoretically preventable although again prematurity creeps in as a factor. Obliteration of the funic circulation is encountered most in prolapse of the cord, either obvious or occult but at least partial occlusion is not infrequent when loops of cord around the neck result in a relative shortening of it so that it is drawn tight during the perineal stage a condition fraught with some danger to the child if there is delay in delivery more likely in a primigravida. A cord complication is always to be suspected if there is no antepartum hemorrhage or prolonged labor to account for signs of fetal distress. Auscultation of the fetal heart should be practiced throughout labor. Special attention to its rate and character is necessary during the half hour that follows rupture of the membranes and during the perineal stage of labor. If the head is high when the membranes rupture, a rectal or preferably a vaginal examination should be made to see if a loop of cord has prolapsed. Early recognition gives the best chance of selecting a successful line of treatment for this complication which is so dangerous for the fetus. A cord drawn tightly around the child's neck is to be suspected if there is a serious reduction in the fetal heart rate or if meconium appears when the head is showing at the vulva. Between pains recession of the head is often considerable because of the relative shortening of the cord. Application of the forceps or an episiotomy or both, to expedite delivery will usually rescue the child. To facilitate auscultation of the fetal heart during this stage of labor it is helpful to keep the patient on her back till delivery is imminent.

A long labor is well known to have an adverse effect on the child. In some cases of prolonged labor the cause of death is cerebral hemorrhage, in others an intrantracheal pneumonia has developed but in the majority asphyxia is the postmortem finding. The mechanism of its production may be that the uterine musculature in time fails to relax completely between contractions, and the resulting increased tonicity produces a prolonged low-grade anoxemia by interfering with the placental circulation and eventually results in intrauterine death of the child. Cruikshank emphasized that direct damage to the respiratory center by edema, produced by prolonged and excessive, increased intracranial pressure rather than gross hemorrhage was the most common post

mortem finding in babies dying of respiratory failure. Holland has suggested crowding down of the medulla oblongata into the foramen magnum as the cause. These dangers are increased if the membranes are ruptured.

Prophylaxis in this group begins with adequate antenatal care so that likely mechanical difficulties in labor such as disproportion and malpresentation are recognized. It becomes necessary to make a very careful assessment in a case of prolonged labor when its duration has exceeded thirty hours. If progress is being made even slowly as judged by improved efficiency of the uterine contractions, increasing dilation of the cervix, and descent of the presenting part and the general condition of the mother and child remain good and a safe vaginal delivery can be visualized further conservatism is justified otherwise an operative delivery should be undertaken. When the head is low in the pelvis and the cervix is more than half dilated manual dilatation or cervical incisions and delivery with the forceps are reasonable. When the head is high the cervix less than half dilated and there is no sign of maternal infection a lower segment cesarean section is called for in the interest of both patients.

Anoxemia due to overdosage with analgesics or the development of cyanosis during general anesthesia are occasional but preventable causes of fetal death.

In the treatment of actually developed intrauterine fetal distress the administration of oxygen to the mother along with a general anesthetic that will inhibit uterine contraction is valuable. When a child showing respiratory failure is born prompt treatment is necessary. The blue and white forms of asphyxia neonatorum are only degrees of the same condition and both may be due to a central or peripheral cause. In both the initial treatment is warmth clearing the air passages with a swab or mucous extractor and gentleness in handling. All methods of artificial respiration are to be avoided as these simply increase shock and may cause actual organic injuries. If there is no satisfactory response and when possible 95 per cent oxygen with 5 per cent carbon dioxide should be administered and 1 cc. of coramine or lobeline hydrochloride (0.003 gm in 1 cc. of sterile water) injected. The passage of a pharyngoscope and tracheal insufflation may be given consideration.

In the maternity-pavilion series of postmortem examinations, cerebral hemorrhage was found in 44 breech 45 forceps, and 50 spontaneous vertex deliveries, as well as in 3 children delivered by cesarean section. As spontaneous vertex deliveries are by far in preponderance and deliveries with the forceps are more than twice the number of breech deliveries, the incidence of this lesion is highest in breech and lowest in spontaneous births.

In the spontaneous group too quick a labor often has subjected the head to too rapidly changing strain and stress. In contrast to too quick labor the excessive head molding associated with a labor prolonged

because of a degree of disproportion can produce laceration at the attachment of the falx cerebri to the tentorium cerebelli even when the delivery is spontaneous.

The obstetrical forceps can damage the cranial contents in three ways. It can be applied to the wrong diameters of the head or be used with excessive force or the head can be extracted too rapidly. The influence of all these is naturally much greater in the less well protected head of a premature fetus. The forceps should, therefore, be avoided except for a sound obstetrical indication. Before applying the forceps to a healthy fetus, one should be as certain as possible that the head can be delivered by this means. Realization of this important decision largely accounts for the replacement of the high operation by the lower-segment cesarean section. When the forceps is applied least damage to the child will result if the blades are placed at the sides of the fetal head so that the ears lie within the fenestrated blades with the occiput anterior. To obtain this good cephalic grip is not always easy if the head has not rotated anteriorly so that the sagittal suture lies in the anteroposterior diameter of the pelvis—a state of affairs found only when the head is on the perineum. Undue haste in the actual extraction has the same effect on the cranial contents as a precipitate labor and this temptation must be resisted.

In breech deliveries the incidence of fetal intracranial hemorrhage is high. It is caused by the un-

molded and often imperfectly flexed head being brought too quickly through the bony pelvis. In a primigravida there is the important additional resistance of the incompletely dilated vagina and vulvar muscular ring.

An important recent additional aid in reducing the risk from or the extent of, intracranial hemorrhage in the newborn is the administration of vitamin K to raise the prothrombin content of the fetal blood. When the occurrence of cerebral damage is likely vitamin K can be given to the mother by mouth or by injection from twelve to four hours before delivery or by injection to the infant after birth.

Fetal deaths and a proportion of neonatal deaths are caused either by hazards that exist before birth or by hazards that arise during birth itself. Their reduction is possible, as other countries have shown, and the ways and means are primarily an obstetrical responsibility. Adequate maternal nutrition so closely linked to improvement in social and economic standards should help reduce fetal deaths by diminishing the incidence of prematurity and possibly limiting toxemia as well as eventually eliminating contracted pelvis. Better practical midwifery in which judgment and technical skill are equally important and necessary in order to deal with difficult and prolonged labor should bring about some reduction in the number of theoretically preventable neonatal deaths.

CHARLES BARON, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY AND URETER

Calp, O. S.: *Renal Ectopia; Report of 6 Cases.*
J. Urol., Balt., 1944, 58: 470.

Six cases of renal ectopia were found among 747 patients who were studied pyelographically during a single year a clinical incidence of 1:125. Most reports indicate that ectopia in its many forms should not be anticipated this frequently.

Three patients had simple unilateral ectopia. Although in 70 per cent of the published cases the ectopia was on the left side, in 2 of the author's group it occurred on the right. The most common location for simple renal ectopia is in the true bony pelvis, but in none of these cases was this location correct. Only 1 of the 3 ectopic kidneys presented secondary disease, but all 3 patients had symptoms referable to the kidney.

Two patients had crossed ectopia with fusion. This anomaly usually is found on the right side. Both of the fused kidneys were on the left. The lower kidney was ectopic in both instances. Secondary disease was present in only 1 case but this explained the symptoms referable only to the upper urinary tract.

One patient had crossed ectopia without fusion. The kidney was hypoplastic also. The normally placed right kidney had duplication of the pelvis and ureter and compensatory hypertrophy. The patient's only symptoms were nocturnal enuresis.

Two of these 6 patients had also congenital anomalies of the skeletal system. No genital abnormalities were present, although they were common in previous reports.

The facts that 2 patients had no symptoms referable to the upper urinary tract and no secondary disease, and that 2 others had symptoms only while the superimposed disease existed, add support to the contention that symptomatology usually is due entirely to secondary changes in ectopic kidneys. However 2 patients with pain reproduced by filling the ectopic pelvis and with no secondary disease, indicated that the ectopia per se may in selected instances be capable of causing discomfort.

JOHN A. LOFF, M.D.

Jacobs, A.: *Transplantation of the Ureters into the Bowel.* *Glasgow M. J., 1944, 143: 97.*

In certain congenital and acquired conditions of the urinary bladder the organ is totally incapable of carrying out its function of retaining urine or it has a capacity which is only a mere fraction of the normal. In the one instance there is complete incontinence and in the other severe day-and-night frequency. When the condition is not amenable to cure, deviation of the urine from the bladder is necessary. In the treatment of primary vesical carcinoma by total cystectomy deviation of the urine is necessarily the

first stage. Nephrostomy and cutaneous ureterostomy are less attractive measures than ureterosigmoidostomy and the author utilizes these measures only as palliative treatment when the life expectancy is not great.

After it has been established that deviation of the urine from the bladder is indicated intravenous pyelograms are made to show the function of the kidneys and the morphology of the ureters. The patient receives a low residue diet for one week and for three days before operation a mild aperient such as petrolagar is given thrice daily. In addition a soap and water enema is given in the morning and a colonic irrigation in the evening. A final lavage is given the morning of operation and the patient comes to the operating theater with the tube in the rectum. Sulfathiazole, 1.0 gm. every six hours in addition to sulfiaguanidine is given for three days preoperatively and the fluid intake is kept at 5 pints.

The operative procedure is fundamentally the Coffey operation No. 1. Through a midline incision the peritoneal cavity is entered and the intestines are packed into the upper abdomen. The posterior peritoneum is incised the ureter is amputated as low as convenient, and a ureteral catheter is inserted. The serosa and muscularis of the pelvic colon are incised for a distance of 2 inches and the ureter is placed in its new bed without angulation. The first row of sutures is placed in the muscularis of the colon to hold the ureter in place. Then the mucosa is incised and the ureter is carried into the lumen of the bowel and held in place by a single gut suture. The distal ureter is incised 1.5 cm. longitudinally to prevent contracture of the orifice. A second row of sutures is placed in the muscularis of the colon, and the posterior parietal peritoneum is closed. Ordinarily both ureters are implanted at the same operation.

Postoperative care involves the use of a rectal tube for six days and a continuous intravenous drip for the first forty-eight hours. About 4 pints of 5 per cent glucose in saline solution and 2 pints of 4.285 per cent sodium sulfate for each twenty-four hours are administered. Pituitrin (3/4 cc. every six hours) has been useful to combat intestinal distention. A mild laxative is given on the fourth day and continued in varying amounts until at least one daily formed motion results. After removal of the rectal tube a variable period of frequency follows, but usually by the end of four weeks an interval of from three to four hours is quite common with a still longer period at night.

The indications for ureterosigmoidostomy are vesicovaginal fistula resistant to surgical repair, vesical contracture due to encrusted cystitis, Hunner's ulcer and tuberculosis, congenital malformation of the urinary bladder, urethral injury beyond

repair and carcinoma of the urinary bladder to be treated by total cystectomy.

The operative mortality in 38 cases was 31.5 per cent, while in 13 cases of vesicovaginal fistula the mortality was only 7.6 per cent. Patients with chronic urinary infections or with tuberculosis or malignant disease are poorer operative risks and consequently a greater mortality is expected.

Following ureterocolicostomy the life expectancy is not appreciably altered. The first patient in the series is alive and well twelve years later. The fear still entertained that transplantation of the ureters must be followed by a serious ascending renal infection with decreased renal function and consequent poor prospects of life expectancy has been greatly exaggerated.

DONALD F. McDONALD, M.D.

BLADDER, URETHRA, AND PENIS

Crisol, D. S., Greene, L. F. and Thompson, G. J.: Interstitial Cystitis of Men. *J. Am. M. Ass.* 1944 36 85.

On the basis of a review of 78 cases of interstitial cystitis in men the following conclusions were drawn:

1. Although interstitial cystitis is predominantly a disease of women it is found to have a significant incidence among men. A search for evidence of interstitial cystitis among male patients will explain a number of cases of puzzling and intractable cystitis.

2. The clinical picture among male patients is often deceiving because of accompanying obstructive symptoms, especially in the prostatic age group.

3. Still more deceiving are the cases in which obstructive symptoms are superimposed without any obstructive pathological change. In those cases the obstructive symptoms are part of the picture of cystitis and will be found to be relieved by treatment of the cystitis rather than by a prostatic operation.

GENITAL ORGANS

Swyer, G. I. M.: Some Observations on the Pathological Anatomy of Benign Prostate Enlargement. *J. Path. Bact., Lond.*, 1944, 56 365.

Observations on the pathological anatomy of prostatic enlargement with particular reference to the etiology were made upon 238 prostatic patients of all ages, of which 119 were forty-six years old or more and presented the changes of benign enlargement.

The uvula vesicae, a median knob of adenomatous tissue behind the internal urethral meatus, was found to arise from laterally disposed adenomas in 11 of the 15 cases in which this structure was present. It was not present in a patient younger than fifty-seven years. In one patient the uvula originated from trigonal glands and in another case from the preperineal glands.

With serial sections the author has demonstrated that in most cases the tubules of the uterus masculinus do not communicate with the adenomas occurring in benign prostatic enlargement. However in some

cases there was an unmistakable intercommunication between the uterus masculinus and the prostatic ducts.

This evidence might be considered to favor the theory that benign prostatic enlargement is due to hyperplasia of the uterus masculinus. However such participation of muellerian tissue cannot be regarded as indispensable since it is observed so uncommonly. It is the author's belief that the earliest changes of prostatic hypertrophy consist of glandular hyperplasia anterolateral to the urethra in the caudal half of the prostate and involving the most medial of the prostatic glands. In the normal prostate of the third and first half of the fourth decade, hyperplasia of the duct epithelium occurs in just such areas. It would appear that benign hypertrophy begins as an intensification of the growth process which subsequently becomes disorganized in those parts of the prostate which possess the highest growth potential, as evidenced by persistence of normal proliferative activity. The fact that such persistent proliferative activity may also exist in the preperineal lobe would account for the participation of that lobe in some, but by no means in all cases of benign hypertrophy of the prostate.

DONALD F. McDONALD, M.D.

Watkinson, J., Delory, G. E., King, E. J. and Hadow, A.: Plasma Acid Phosphatase in Carcinoma of Prostate; Effect of Stilbestrol. *Brit. M. J.* 1944 2 492.

The authors present details of the method employed for the estimation of acid phosphatase, and of the values obtained for plasma acid and alkaline phosphatase in various clinical conditions and in normal controls, and for acid phosphatase in seminal fluid. Two specimens of seminal fluid from a case of eunuchoidism contained relatively negligible amounts of acid phosphatase.

Of 10 cases of prostatic carcinoma, 6 showed a raised acid phosphatase content in the plasma and in 5 of these there was roentgenographic evidence of metastases in bone. Several of the results do not show any marked distinction between prostatic carcinomas with metastases and Paget's disease.

The behavior of the plasma phosphatases in cases of carcinoma of the prostate in which the plasma acid phosphatase was originally raised was followed during treatment with stilbestrol. The response shows a uniformity of pattern, the acid phosphatase falling abruptly to a normal level, which is then maintained for considerable periods, with a rise in alkaline phosphatase followed by a gradual fall.

Of 10 cases of carcinoma of the prostate, 4 showed some degree of regression of the primary tumor under treatment with stilbestrol, and secondary deposits in lymph nodes underwent regression in 3 cases. X-ray examination at three-monthly intervals in the cases with metastasis to bone revealed in some a progressive increase in density while in others the deposits became more numerous during treatment or increased in size.

With one exception all cases showed some measure of symptomatic and general improvement, in relief from pain, decrease in the frequency of micturition or gradual increase in the hemoglobin level and in improvement in appetite and gain in weight.

JOHN A. LOER, M.D.

Franklin, A. P.: Reconstruction of the Male Genitalia. *Am Rev Seriol Med.*, 1944, 2: 14.

The smallest remnants of the cavernous bodies must be utilized in the reconstruction of the penis in such a way that the erectile functions may be transmitted to the new organ and thus make sexual activity possible. In reconstruction of the urethra, the method used is that developed and reported by Bogura (*Zentralbl Chir* 1936 63: 1 271) but under much more difficult conditions. The operation is performed, as a rule, in four stages: (1) formation of an abdominal skin tube into which rib cartilage is inserted, (2) transfer of the proximal pedicle of the tube and implantation of the cartilage into the remnants of the cavernous bodies, (3) division of the distal end of the tube and formation of the penis and (4) reconstruction of the urethral canal, either as a pedicle from the scrotum immediately beneath the reconstructed penis, its under surface thus becoming the upper wall of the new urethra, or by such a flap taken from the fine skin of the upper arm, or other where.

By this implantation of the cartilage the tumefaction under the influence of the sexual impulses moves the cartilaginous portion of the penis upward and forward so that coitus is possible. During sexual stimulation a light erythema and swelling of the reconstructed penis occurs. At first the absence of the glans penis results in very weak orgasms and ejaculations in time however new erotic zones apparently develop and the orgasm approaches normal intensity.

In summary it may be confidently stated that a procedure which permits reconstruction of a normally functioning genital organ is an important contribution to modern plastic surgery.

JOHN W. BRENNAN, M.D.

MISCELLANEOUS

Beigel, W. T.: Sterile Pyuria. *J Urol.*, Balt. 1944, 52: 283.

"Sterile pyuria" is being recognized as a definite clinical entity. The evidence at hand suggests as the etiologic agent a Gram positive coccus which fails to grow on the usual culture media. The sulfonamides are of little avail in this condition.

The author presents 4 cases with similar histories, findings, and response to treatment. Salient features of the disease are complaint of long standing day and night frequency of urination in an adult accompanied by dysuria and tenesmus. Typically the urine shows 2 to 4 plus albumin, 2 to 4 plus pus and 0 to 1 plus red blood cells with no bacteria apparent on stained smear or upon routine culture. Cystos-

copy and pyelography are uniformly negative. Treatment with sulfonamides is uniformly unsuccessful, whereas 3 or 4 injections of 0.3 gm. of neoarsphenamine are attended by rapid symptomatic and objective improvement. In 1 of the 4 cases Gram positive cocci in chains appeared in the urine following arsenical therapy. The author believes that the appearance of staphylococci after one or more doses of neoarsphenamine in no way makes the diagnosis of sterile pyuria incorrect.

In these 4 cases the results of treatment were rapid and complete. Recurrences have not occurred over follow up periods for as long as five years.

The author concludes that "sterile pyuria" is a definite clinical entity simulating renal and vesical tuberculosis in its symptomatology. The cause of sterile pyuria is probably an organism of the coccus group difficult to grow and hard to find in stained smears. It is probably not a virus since virus diseases do not respond to the arsenicals. It is seldom cured by the urinary antiseptics including sulfa drugs usually employed in renal and bladder infections but responds sometimes in a spectacular manner to arsenicals.

DOMALD F. McDONALD, M.D.

Scarcello, N. S.: Penicillin in Sulfonamide-Resistant Gonorrhea. *N England J M.*, 1944, 231: 609.

The author reports a carefully analyzed series of 200 cases of sulfonamide resistant gonorrhea which were treated with variable initial doses of penicillin ranging from 150,000 to 30,000 units. Fourteen per cent of the cases required two or more courses of penicillin. There were no failures in this group of cases treated and the patients were returned to duty in one-third of the time usually required.

When 100,000 or more units of penicillin were exhibited initially only 9 per cent of the cases required repeat courses while when 80,000 or less units of penicillin were used 17 per cent required repeat courses of penicillin.

In the group treated there were 3 with complicating gonorrheal arthritis and this cleared rapidly with penicillin. Four individuals with prostatic abscess showed immediate improvement with the use of penicillin but the drug seemed to have little or no effect on a complicating epididymitis. No toxic reactions to penicillin were experienced.

The author warns that penicillin may mask the presence of primary syphilis. It is further suggested that although sulfonamides may not affect a case of gonorrhea in an individual, their continued use until penicillin is obtainable will assist in localization of the disease and thus afford a more rapid cure with penicillin.

ROBERT LICH, M.D.

Eagle, H.: The Treatment of Early and Latent Syphilis in from Nine to Twelve Weeks with Triweekly Injections of Mapharsen. *J Am M Ass* 1944 136: 538.

The three major considerations of chemotherapeutic procedures determining dosage and duration

of treatment of syphilis with mapharsen are therapeutic efficacy, toxicity and practicability. Studies on experimental rabbit syphilis revealed that the total curative dose is relatively constant. The toxicity varied directly with the method of administration. These relationships also hold in man. Weekly doses of 60 mgm. are attended by a mortality of 1 in 5,000, whereas when the total dose is given in five days the mortality has been 1 in 500. It was thought that triweekly injections of about 1 mgm. per kilogram would result in a mortality less than 1 in 1,000 and a course of treatment which would last but from nine to twelve weeks.

The clinical study was commenced in 1941 with the co-operation of venereal-disease clinics. With a few exceptions all patients were ambulatory. The dose of mapharsen was between 40 and 80 mgm. (adjusted to body weight) and averaged 60 mgm., this was given three times a week. The duration of treatment varied from four to twelve weeks. About half of the clinics also gave an injection of bismuth each week. Clinics were urged to give quantitative serological tests at least twice during the course of the therapy and monthly thereafter. A spinal puncture three and twelve months following treatment was advised.

Of 4,813 cases treated there were 90 with seronegative primary syphilis, 1,054 with seropositive primary syphilis, 2,050 with secondary syphilis, and 1,190 with latent syphilis. There were 151 patients previously treated for syphilis who were now diagnosed as having an infectious or serological relapse, and 8 with late recurrent syphilis. Forty per cent of the total were white and 53 per cent were male. In evaluating response to treatment, infectious relapse, clinical or serological evidence of central-nervous-system involvement, serological relapse and cases presenting persistently positive blood serology were adjudged as treatment failures. Cases which were strongly suggestive of reinfection rather than relapse were also considered treatment failures.

Evidence of minor toxic reactions consisting of nausea, vomiting, malaise or headache occurred in 16 per cent of the patients and approximately 15 times more frequently in women. In 33 patients or in of every 210 treated repetition of these minor reactions made it necessary to discontinue treatment. In 106 patients a syndrome suggesting sensitization to mapharsen was observed. Reactions in the order of decreasing frequency were fever, rash, vomiting, headache, conjunctivitis, photophobia, and facial edema. Recovery was usual in from forty-eight to seventy-two hours. In a total of 54 patients it was necessary to discontinue treatment. Serious reactions occurred in a total of 39 patients. They consisted of 2 cases of toxic encephalopathy (1:2,400), 7 cases of arsenical dermatitis (1:950) and 21 cases of jaundice (1:15). Seventy-five per cent of these reactions occurred in the second to fourth week of treatment. There were 4 deaths (1:1,500): 2 due to nephritis, 1 to encephalopathy and 1 to jaundice. In 2 or perhaps 3 of these cases death may have been

preventable. Serious toxic reactions tended to occur in young women and negroes. The 4 deaths occurred in negro women 3 of whom were under eighteen years of age.

Therapeutic results in early syphilis when mapharsen alone was given were uniformly poor, with from 9 to 15 per cent failures. When bismuth was also given failures occurred in from 11 to 6.6 per cent. The addition of only 5 injections of bismuth to the smaller amount of mapharsen (less than 21 mgm. per kilogram) increased the fifty to sixty-week "cures" from 49 to 65 per cent.

When 21 mgm. or more of mapharsen per kilogram were supplemented with an average of 9 injections of bismuth, seventy-week "cures" were obtained in 82 per cent. Thus, triweekly injections of from 40 to 80 mgm. of mapharsen combined with weekly injections of 0.2 gm. of bismuth subsalicylate for from nine to twelve weeks will "cure" from 80 to 90 per cent of the cases of early syphilis.

Infectious relapse and serological relapse accounted for 43 and 40 per cent of the failures respectively. Involvement of the central nervous system accounted for 13 per cent of the failures, and 7 per cent of the failures occurred in patients whose positive serology was at a stationary level one year after treatment. The present study gave no indication of a more favorable prognosis in secondary syphilis. In patients with previously treated early syphilis who had relapsed, the number of treatment failures was no greater than in previously untreated cases when both bismuth and mapharsen were given. Good results were obtained with the intensive treatment schedule in latent syphilis. The rate of serological reversal was found to depend upon the initial serological titer but the latter had no effect on the prognosis for early syphilis.

DONALD F. McDONALD, M.D.

Goodall, J. R.: Urinary Complications of Pelvic Endometriosis. *Ann. Surg.* 1944, 70: 891.

Secondary endometriosis seldom involves the urinary organs, but involvement of the urethra, bladder and ureters is reported. The type and degree of involvement of the urinary tract depends upon (1) the histological type of cell involved, and (2) the mode of invasion of the urinary tract.

Stromatous endometriosis arising from non-glandular connective tissue elements of the deep layers of the endometrium does not undergo change with the menstrual cycle. This type of endometriosis secondarily involves the trigone and base of the bladder when there is direct lymphatic continuity with the uterus. The author describes 2 cases of this type in which the whole pelvis was invaded and there was loss of sphincter control with incontinence and cystitis. Mixed glandular and stromal endometriosis arising from the superficial layers of the endometrium undergoes cyclical response with the uterus. This type of endometriosis involves the bladder by implants in the peritoneal vesicouterine pouch and also by traumatic displacement of endometrial tissue to

the peritoneal surface of the bladder following surgery in cases of endometriosis. In 30 per cent of these cases previous pelvic surgery for endometriosis had been performed. As most of these cases are derived from intraperitoneal disease incident to total regurgitation of endometrium they respond to the menstrual cycle and rhythmic hematuria is the most efficient sign of bladder endometriosis. Cystoscopically there is a bladder growth surrounded by edema, congestion and blue grapelike masses. During menses, edema and congestion increase and there is marked hemorrhage. The lesions are predominantly in the dome of the bladder. This picture is in contrast to that found in stromatous endometriosis in which the trigone is involved by pearly white cystic growths varying from the size of a millet seed to that of a bean which do not change in appearance during menses.

The author describes secondary mixed endometrios of the urethra which underwent cyclic changes and responded well to local excision and pelvic irradiation. He also describes secondary involvement of the ureters by ectopic endometrium in 4 cases. Two patients with stromatous endometriosis lived eleven and twelve years after diagnosis with temporary benefit from roentgen irradiation followed by gradual invasion of all the pelvic structures and death due to uremia consequent to ureteral obstruction. Two cases of mixed endometriosis involving the ureters had the presenting symptom of pain in the flank due to hydronephrosis. Treatment of secondary endometriosis involving the urinary tract is similar to the usual treatment of endometriosis. Partial cystectomy for lesions involving the bladder is not recommended.

DONALD F. McDONALD, M.D.

Cannon, A. B., Fisher, J. K., Rodriguez, J. J., Beattie, G. F. and Macchilling, E. *Intensive Arsenotherapy* *J. Am. M. Ass.* 1944 126 544

In the past three years 332 cases of early syphilis in chiefly healthy young men were treated with massive doses of arsphenamine by the syringe method, the treatment period extending over five or six days. Two-thirds of the patients were negroes. All of the patients were hospitalized and given complete physical and laboratory examinations, including quantitative Wassermann tests on serum and spinal fluid, blood and platelet counts, serum bilirubin and urea and cephalin flocculation tests as well as daily determinations of the blood arsenic levels. Frei and Dreyer tests and urethral cultures were made in all

cases. Daily dark field examinations and urinalyses were performed. After discharge from the hospital the patients were seen at weekly intervals in the clinic for the first six weeks and then at monthly intervals.

Treatment consisted of the intravenous administration of a 2 per cent solution of arsphenamine three or four times a day for five or six days according to one of seven plans. The total dose varied from 1.5 gm. to 4.4 gm.

Seven treatment plans were used each new plan having been worked out after analysis of the results of the preceding plan. It was determined that in order to make the dark field examinations negative in twenty four hours it was necessary to give 1.0 gm. in the first day. Healing of surface lesions was prompt and usually complete in one week. Of 332 patients treated only 178 have been followed up from six months to three years. Of these, 118 or 66 per cent were clinically and serologically negative and had normal spinal fluids. Mucocutaneous relapses occurred in 9 cases and failure of the serology to become negative in one year occurred in 12 cases.

There were 12 severe reactions: 1 ending fatally. These included 2 of encephalitis, 3 of hepatitis (1 fatal), 2 of exfoliative dermatitis, 3 of persistent neuritis and 2 of blood dyscrasias. There were numerous minor reactions such as an initial rise of the temperature on the first day which subsided the next day. Secondary rises in temperature and toxic erythemas occurred near the end of the course of treatment, and mild neuritis usually appeared about two weeks after cessation of treatment. As the amount of drug was increased the occurrence of secondary fever increased from 15 per cent to 80 per cent, mild neuritis increased from 2 per cent to 35 per cent and toxic erythemas increased from 8 per cent to 40 per cent. Trace albuminuria was present in 18 per cent. Vomiting occurred in 22 per cent, and diarrhea was present on the first day in 10 per cent.

Laboratory studies of the blood arsenic levels showed that there was always a retention of arsenic long after cessation of treatment. Reactors showed a greater retention of arsenic and for a longer period of time than nonreactors, and the more arsenic received the greater was the retention.

The authors conclude that treatment of early syphilis with arsphenamine by the multiple syringe method over a period of five or six days is ineffective, dangerous, expensive and altogether impractical.

DONALD F. McDONALD, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Wang, K. Liu S. H. Chu, H. L. Yu T. F. and Others: Calcium and Phosphorus Metabolism in Osteomalacia. The Availability of Inorganic Phytin, and Dietary Phosphorus and the Effect of Vitamin D. *Chin. M. J.* 1944, 69

Phytin, the calcium and magnesium salt of inositolphosphoric acid (phytic acid) is a relatively poor source of phosphorus for absorption and utilization by the human organism. Phytic acid is widely distributed in foodstuffs, especially in cereals, in which it constitutes from 50 to 70 per cent of the total phosphorus. It is assumed that phytin is of limited value nutritionally.

McCance and Widdowson who calculated the phytin portion of total phosphorus in the diets of the moderate class population in England, gave an average figure of 5 per cent. In China, ordinary diets are largely composed of cereals. Yang and Dju estimated that in some typical diets in Shanghai, from 24.5 to 50 per cent of the total phosphorus was in the form of phytic acid. In northern parts of China where osteomalacia is prevalent, cereals constitute the main dietary staples. A high cereal diet is not only low in calcium it is high in phytic acid. It is possible that a dietary intake of phosphorus, largely in the form of the relatively unavailable phytic acid, plays a role in the pathogenesis of osteomalacia. The present article deals with the availability of phytin phosphorus in patients with osteomalacia.

Two cases of osteomalacia were studied to ascertain the availability of phytin phosphorus supplied either from cereals or from phytin preparation as compared to its availability when inorganic phosphate (constant calcium and constant total phosphorus) was administered.

When from 30 to 40 per cent of the phosphorus intake was in the form of phytin the absorption and retention of both calcium and phosphorus were decreased, when compared with the absorption and retention following a similar level of intake of inorganic phosphorus. The impaired utilization of phytin was due to its limited hydrolysis and to the incomplete absorption of hydrolyzed phytin. Vitamin D while unequivocally capable of promoting the absorption and retention of calcium and total phosphorus, did not show a clear-cut enhancing effect on the utilization of phytin. A high cereal or phytin-containing diet is believed to be an important factor in the pathogenesis of osteomalacia.

The primary purpose of this investigation was to ascertain the role of a high cereal or phytin-containing diet in the pathogenesis of osteomalacia. Numerous studies have made it clear that osteomalacia

is primarily due to vitamin D deficiency and that factors like the low calcium Chinese diet and the excess mineral drain from repeated pregnancies and prolonged lactation play contributory but important parts in making the condition especially prevalent in China. The relatively high total phosphorus content of ordinary Chinese diet has hitherto conveyed an impression of adequacy of phosphorus intake, and any deficiencies in the absorption and retention of phosphorus were regarded as secondary to vitamin D deficiency and calcium shortage. However the present work indicates that the form of phosphorus supplied is significant. The results presented confirm the observations of previous workers in animal experiments that whenever phytin constitutes a considerable proportion of the phosphorus intake, the absorption and retention of phosphorus are much less than when a similar level is administered in the form of inorganic phosphorus. This impairment of phosphorus metabolism is accompanied by a decrease of calcium absorption and retention.

ROBERT P. MCCORMACK, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Gold, C. W.: The Os-Purum Implant. A Substitute for the Autogenous Implant. *J. Bone Surg.* 1944, 26: 758.

In the author's experience with os-purum implants, the following conditions were noted:

1. All osteogenic sources about the recipient bed must be carefully preserved.
2. Complete fixation of the parts must follow implantation with os purum.
3. Complete asepsis with the Lane technique is preferred. (In many of the author's cases sulfanilamide powder was sprinkled into the wound before it was closed without any appreciable slowing in the rate of acceptance.)
4. Intramedullary fixation can be used in selected cases without complicating the result appreciably.
5. The implant should remain in its bed for six teen weeks, even if there are signs of intolerance or of foreign-body reaction. By that time it has served its purpose and can be removed.
6. The implant should be shaped to the desired size as carefully as possible. An excess amount of os purum appears to take a long time for absorption, and may produce a slight serous discharge for several months at the site of the wound. This occurred, however in a very limited number of cases. Removal of the implant, or of the excess of the implant, will not interfere with bone formation, and the wound will close promptly.
7. Os-purum implants unless under physiological stress and strain and surrounded by osteogenic tissues will be resorbed and disappear.

Details of the cases used for this report are included. The author believes that the use of os purum has its place, and that os purum constitutes a satisfactory material for the orthopedic surgeon. For the duration of the War however it appears that os purum cannot be obtained from Sweden. The supply in this country is almost exhausted. Perhaps some biochemical manufacturer may see fit to produce os purum in this country if this can be done under trade agreements.

Leriche and Pollicard pose three propositions to be fulfilled for the future of bone surgery: (1) Can one influence the formation of bone? (2) Can one influence bone resorption? (3) Can one model new ossifications? The use of Orell's especially prepared bone introduces a substance which promises to go far toward answering these three interesting questions.

ROBERT P. MORROW, M.D.

Harris, R. L.: Amputations. *J Bone Surg* 1944, 26 625.

One of the most admirable surgical chapters of the last war was written on the subject of amputation. Separation of amputees concomitant with the installation of many amputation centers in Canada, England, and the United States is a product of this war. Much of the efficacy of the modern prostheses worn by amputees today is attributed to a clearer understanding between the surgeon and the limb maker.

The author has conveniently divided amputations into two stages: (1) the field stage, which is performed at or near the zone of combat and (2) the second stage, which is performed in the zone of the interior at some amputation center.

In the field, the amputation may be performed for a grossly infected limb, the removal of an irretrievably damaged limb, a massive wound caused by shattering missiles, irreparable circulatory damage and, lastly, to save the soldier's life. The governing principles of field amputation postulated by the author are as follows: (1) save as much of the limb as possible, (2) perform judicious débridement, (3) control infection, (4) manage the stump as an open wound, (5) enhance the healing, and (6) prevent flexion deformity of the stump. Amputation should be performed at or above the line of demarcation in all limbs exhibiting circulatory incompetency. The guillotine or modified guillotine operation is the operation of choice. Skin traction should be applied early to augment healing, except in cases with highly contaminated limbs in which one must await subsidence of the infection.

In the second stage, definitive treatment of an amputation is instituted; this is possible after the wound has healed at the amputation center. The operation must achieve as its objectives: primary healing, a perfect usable stump, an optimal level of function and a stump ready for prosthetic appliances.

The author describes and recommends four types of standard amputations of the lower extremity: (1)

Syme's, (2) below the knee, (3) Stokes-Griffith and (4) midhigh amputation.

Syme's amputation is the most serviceable operation involving the foot. If any imperfections ensue in a Syme's stump they are due to failure to secure primary healing, supervening infection, or displacement of the heel flap resulting from tissue redundancy. While Syme's stump is amenable to useful prostheses in the male, it is esthetically displeasing to women as it is notoriously bulbous.

Below-the-knee amputation differs mechanically from Syme's amputation in that the weight is borne by the flaring sides of the tibial condyles. This stump yields greater usefulness if the amputation level is no longer than 7 inches and no shorter than 5 inches from the upper border of the patella. If one has no alternative, even a 3 inch stump is better than a disarticulation. Occlusion of sebaceous glands and hair follicles with circulatory disturbances may cause cutaneous infections and therefore impair weight bearing. Scrupulous attention of the stump postoperatively is tantamount to the surgical interference.

The Stokes-Griffith amputation is the operation of choice above the knee. It yields excellent weight bearing qualities. If the femoral condyles are greatly damaged or the patella with its cutaneous envelope is irretrievably injured, then it becomes mandatory that a midhigh amputation be performed. The cut end of the femur must conform to the hemisection of the patella in the Stokes-Griffith amputation.

Midhigh amputation is to be performed in cases in which the Stokes-Griffith is inadequate. Weight bearing in this stump may be equally divided between the ischial tuberosity and the distal stump. The ideal length of the stump is 11 inches from the greater trochanter. It is necessary that the skin, fascia, muscles and bone be cut at successively higher levels. The stump should be of a conical shape and devoid of redundant tissue.

Reconditioning includes the efficient use of prostheses, avoidance of infection and flexion deformity and the maintenance of balanced muscle power by physical therapy. SAMUEL L. GOVERNALE, M.D.

Bosworth D M.: The Posterior Approach to the Femur. *J Bone Surg* 1944, 26 637.

The posterior approach to the femur has been used for the following:

1. Open reduction of malunion and nonunion of fractures of the middle third of the femur.
2. Biopsy and removal of tumors in that area.
3. Femoral shortening.

A posterior midline incision is made. The linea aspera is exposed by blunt dissection. The long head of the biceps is retracted medially for the exposure of the upper third of the femur, retracted laterally for exposure of the lower third of the femur, and divided at its distal end and retracted medially for exposure of the entire femoral shaft. There has been no instance of damage to the sciatic nerve caused by this surgical approach. Bleeding of any conse-

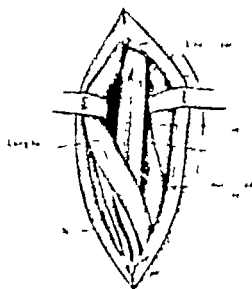


Fig. 1. For removal of the middle three-fifths of the femur the long head of the biceps is retracted medially.

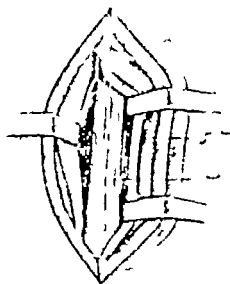


Fig. 2. For the long portion of the middle three-fifths of the femur the long head of the biceps and the sciatic nerve tract of the leg are retracted laterally.

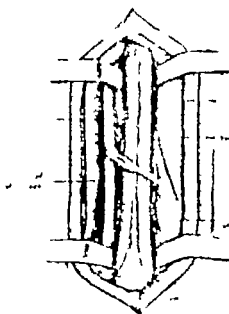


Fig. 3. For complete exposure of the middle three-fifths of the femur the long head of the biceps is retracted medially, and, with the sciatic nerve retracted laterally.

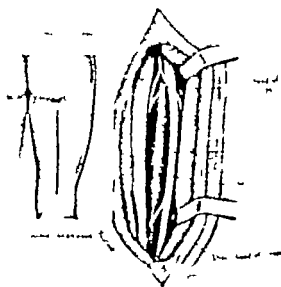


Fig. 4. The entire middle three-fifths should never be exposed by lateral retraction of the biceps, as the sciatic nerve will be left exposed to damage. Insert: Line of incision for exposure.

sequence was encountered only when muscular attachments to the linea aspera were freed by sharp dissection. The operation is completed by suturing the

skin only, allowing the other structures to fall back into place. Excessive formation of fibrosis is thus prevented.

GEORGE L. REISS, M.D.

FRACTURES AND DISLOCATIONS

Howard J. E. Winternitz, J., Parson W. Bigham R. S., Jr. and Eisenberg, H.: Studies on Fracture Convalescence. The Influence of Diet on Post Traumatic Nitrogen Deficit Exhibited by Fracture Patients. *Bull Johns Hopkins Hosp* 1944, 75 209.

The authors present a continuation of their studies on nitrogen metabolism in patients convalescent from fractures of the large bones of the lower limbs. In their previous communication they stated that large losses of body nitrogen were incurred following such fractures and that even after nitrogen equilibrium was regained repletion of the lost nitrogen took place at a very slow rate.

In the present report the authors attempt to evaluate the role of diet, especially protein intake, in the nitrogen loss suffered by these patients. Control studies of the expected nitrogen loss were first carried out on normal healthy individuals at bed rest on a given dietary intake. The loss was found to be very small these individuals having a negative nitrogen balance of from 5 to 20 gm per day.

Following fracture, however and irrespective of the quantity of protein nitrogen in the diet, there occurred a definite loss of the nitrogenous portion of large amounts of body protein. Ingested increments of high protein food or even of amino acids did not spare the utilization of body protein. This type of reaction seemed to demand that a certain amount of endogenous protein be catabolized and that additional dietary protein beyond a certain minimum be demineralized without serving a sparing effect on the body nitrogen stores.

As convalescence proceeded the protein-catabolism phase of this process diminished and the amount of ingested protein influenced more and more the overall nitrogen balance, tending to span the body protein and bring about a positive nitrogen balance. The fact that this protein catabolic process occurred soon after injury in healthy vigorous subjects but not in all subjects, has led the authors to suggest that this process may be helpful in some way to the individual, and that a patient capable of responding to trauma with a vigorous protein catabolism is a better "surgical risk" than one who is unable to respond in this manner.

DANIEL H. LEVINTHAL, M.D.

Leavitt, D. G. and Woodward, H. W.: March Fracture. A Statistical Study of 47 Patients. *J Bone Surg.* 1944, 26 733.

March fracture is a fissure fracture due to stress which most commonly occurs in the second third or fourth metatarsal bones, but may occur elsewhere. It is not produced by a single injury or accident. The etiology is represented by a combination of external and intrinsic circumstances which weaken the fore foot. Roentgenograms made before healing begins may show no evidence of fracture. In the later stages, callus formation and a fracture line are usually found. If no treatment is given angulation displacement, and excessive callus formation may occur.

The authors discovered that many accepted concepts were disproved and that patients had serious disability which tended to be recurrent and prolonged. Many were lost to the combat unit permanently.

The authors state that their data showing a gradual onset in 52 per cent of the cases is misleading because the soldier knows the date and stage of the march at which the symptoms began.

The atavistic foot has either varus of the first metatarsal shortening of the first metatarsal or increased flexibility of the first metatarsocuneiform joint or all of these characteristics which are predisposing factors. The high incidence (50 per cent) of normal foot posture, and the presence of varying degrees of pes cavus in 32.5 per cent of instances were unexpected.

The predisposition through congenital structure of the foot, is again indicated by the bilateral march fractures and the occurrence of refracture or multiple fractures in one foot.

Since the congenital features in the so-called normal asymptomatic soldiers are not known the authors cannot properly stress their contribution to the etiology but they no doubt, are basic etiological factors in the occurrence of march fractures.

There are many predisposing factors in march fractures, some of which, it has been found may be controlled.

Difference of opinion exists as to the desirability of suppleness in the sole of the foot. For ordinary walking it seems excellent but when a heavy pack is added a more rigid sole offers protection against excessive localized bending stress.

Training is most important. Foot and general conditioning can be obtained as effectively on soft or natural ground. Combinations of training on hard and soft surfaces should be arranged to properly adjust these factors.

Initial roentgenographic examination is often negative and should be repeated. In 8.5 per cent of the patients no fracture line accompanying the callus formation was visible at any time.

At present the authors believe that early diagnosis and treatment by absolute freedom from weight bearing until soreness disappears may give the best results.

The type of treatment and the end results, reported previously in the literature have not been clearly described.

The end-results reported in this study have been poor. The authors conclude that march fracture in soldiers is more serious than other reports have indicated.

Most patients returned to light duty with their organizations while wearing unpadded plaster casts. They appeared to do little better than did those with unrecognized or late untreated fracture, or the few patients who though seen early were untreated by choice. These poor results appeared despite the fact that weight bearing in plaster is one of the accepted forms of treatment.

In all war zone and unrequited cases. If a third of the soldiers with complications in which the patient returns, the other have in a tied up or isolated condition. The patient is kept in bed for a week, the plaster is changed a plaster applied three weeks with a light bearing on the plaster. A daily bath is necessary for a couple of weeks. At the end of the plaster period, a simple bath is the duration is over two weeks warm whirlpool bath and massage treatment are given daily and continued with the light bearing until the patient appears comfortable walking and as a fact, they are gradually increased if pain is not present.

In all three reports the author would present a series of cases to the medical staff.

R. A. P. M. and R. M. D.

Dew W. A. and Wood, J. H. March Fractures, A Series of 55 Cases. *J. R. A. M. Corps* 1941 31: 332.

The author presents a series of 55 metatarsal march fractures and reports that the majority of patients failed to develop any preexisting foot pathologies. March fractures are attributed to the carrying of the full weight of the foot and marchers are more common in the lower extremities.

In most cases, the fracture is painless and the patient is able to walk. The maximum weight of the foot is usually limited at the second or third metatarsal head. As a rule, the fracture is a hairline fracture, which is able to be treated by a cast. The patient is usually asymptomatic with a little discomfort in the placement of the foot. Only a few patients of the cases necessitated hospitalization. The author states that the hospital was approximately 10 days. The out-patient group required only a few days of rehabilitation.

Local treatment in the mild cases consists of the use of a cast for seventy-two hours, a whirlpool bath, and massage and crutches under the foot bearing within pain limits. Splinting of any form is not advised because of the ongoing stiffness of the foot and increasing morbidity. The prophylactic measures advanced by the authors have met with the most high incidence of march fractures. They recommend a gradual lengthening of the march, progressive increase of heel girth, and what is most important, that the soldier march on the soft shoulders of the roads or across the hills.

SEYMOUR L. GORVATSKY, M.D.

Wilson P. R.: March Fractures: A Series of 64 Cases. *J. R. A. M. Corps* 1941 31: 157.

March fractures were described as early as 1855. By analyzing some 64 cases, the author hopes further light may be thrown on the etiology, treatment, and prevention of the condition. The present series all occurred in young soldiers undergoing a course of training at an Army physical development center. Each course at the center lasts about two months.

The essence of the author's program was graduated physical development. The patient must be taken once a week, starting with three or five miles and working up to eight miles in the last week before and in the final week there is a full on-mile march on each of two consecutive days. For the first few weeks the trainee carries no pack or rifle, but there are added to his load in the two months of training.

As a result of his study, Wilson believes that the incidence of march fracture in the present war is probably higher than for previous cases would indicate. The main factor in etiology, as it appears to be, is a poorly developed crust with poor muscle tone, (b) an unusually high ratio of rigidity to load carried, and (c) a tendency to repeat foot strain and (d) previous and repeated foot strain and (e) changes to the Army boot.

Amputation is almost never indicated early in all cases, the main advantages being an early return to full duty, counteracted by satisfactory healing and ultimate foot function, the limitation of hospitalization, and the elimination of repeated amputations of the foot and the physical and military training.

The possible prevention of the condition of march fracture is a point he is attempting to bring to the proper physical development of the foot and early attention to the condition, using special exercises to develop and strengthen the foot. Adequate care, such as vitamin and mineral should be given.

The tempo and duration of the recruit's training should be geared according to his physical standards. Furthermore, he should be allowed a few weeks to accustom himself to the training with march boots. Army boots are and accurate foot fitting at the outset is essential.

In all cases of pain in the foot following a march strain, such a measure, the possibility of march fracture should be borne in mind. The case may well be present a symptom of the foot, but if it is not being a characteristic, the patient may at first show nothing, and should be reported in all doubtful cases in two weeks.

LESLIE C. HARRISON, M.D.

ORTHOPEDICS IN GENERAL

Schwartz, R. P., Bowman, H. D., and Smith, W. R.: The Significance of Muscle Spasm in the Late Stages of Infantile Paralysis. Based on Follow-up Records. *J. Am. M. Ass.* 1941 63: 1001.

The authors review the literature and the theories regarding the behavior of the neuromuscular mechanism in the acute stage of infantile paralysis. In attempting to differentiate and evaluate muscle spasms and muscle spasm, they studied a total of 50 individuals employing action-current records as their most useful evidence. The 50 individuals studied included 10 normal subjects, 9 patients with spastic paralysis, 6 patients with infantile paralysis, 23 and miscellaneous patients 12.

The evidence collected by these action-current records indicated that during the acute stage of in-

infantile paralysis spasm is present in both weakened and normal muscles when they are stimulated by the stretch reflex. During the postacute stage this spasm diminishes and action-current records made years after the onset of this condition revealed weakness of voluntary contraction without evidence of spasm. In no instance was spasm found when a muscle failed to produce a record of reaction to voluntary movement.

It is the author's opinion that spasticity is a generalized phenomenon in the early stages of infantile paralysis and that there is no correlation between the degree of spasm and the incidence of muscle weakness or paralysis.

DANIEL H. LEVINTHAL, M.D.

Kark, W.: Foot Strain in Services. *J. R. Army Med Corps* 1944, 83: 166.

The author believes that about 1 of every 4 or 5 surgical (soldier) outpatients presents himself because of foot strain and that approximately half of these patients have mild structural deformities. The clinical picture is essentially the same whether the anatomical structure is normal or altered. He then

discusses the incidence of the common deformities and their place in the fatigue syndrome of the foot. Deformities are probably the sequelae of foot strain in a much larger proportion of cases than was considered proved in this series. It is practical to regard all cases primarily as the result of muscular fatigue from overuse and to treat them from this point of view.

The author has found that the adoption of this attitude is emphatically indicated by the almost uniform failure of boot wedges, bars, and arch supports and the patent evidence that the minor foot operations of civilian practice produce major disabilities in service personnel. Adequate foot hygiene and thorough early treatment of minor ailments and injuries are essential measures in the reduction of the incidence of foot strain. Further reduction can be achieved by more gradual and selective training, the essence of the problem being to educate muscles whatever the anatomical form of the foot. The treatment of acute and chronic foot strain is considered in three stages: absolute rest in bed, active exercises in bed, and lastly the stage of weight bearing exercises. Adequate treatment requires hospitalization for from two to six weeks. EMIL C. RONTGEN, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Duncan, G. W.: Venous Pressure as an Index of Blood Flow in the Upper Extremity. *Arch. Surg.* 944, 40-45.

In 1909 a method of determination of the rate of blood flow in the arm was described. It consisted essentially in placing the upper extremity in a plethysmograph and measuring the initial increase in volume of the limb when the venous outflow was occluded by a pressure lower than the diastolic pressure. This principle has more recently been applied to finer methods of determining the rate of blood flow in both the upper and lower extremities. Since vascular engorgement of an extremity is obvious when venous occlusion is produced, the idea suggested itself that measurement of the rate of rise in the venous pressure in one of the large veins of the forearm might be to some degree indicative of the rate of blood flow in the extremity. The author describes in detail the method used in measuring venous pressure as an index of the rate of blood flow in the upper extremity.

Venous occlusion was obtained by an ordinary blood pressure cuff, applied about the upper part of the arm. The pressure to which the cuff was raised was in all cases approximately 10 mm. of mercury below the previously measured diastolic pressure. The remainder of the experimental procedure was then carried out by two different methods. In the first the blood-pressure cuff was rapidly inflated to the desired level by means of a hand bulb while in the second the cuff was more rapidly inflated from a 15 gallon (58-liter) bottle reservoir. Tabulations were presented giving the results of the experiment with both methods. The results of the methods were similar.

These observations indicate that the rate of rise in venous pressure in the large veins of the forearm reflects to some degree the rate of blood flow in an extremity. When the vein of an extremity is suddenly occluded by a pressure lower than the diastolic pressure the arterial inflow continues. The incoming blood progressively distends the arterial, capillary and venous systems which increases the volume in the arm. The initial rapid arterial inflow represents the normal rate of inflow. Gradually this rate decreases as the pressure rises in the capillary and venous systems. The rise in pressure in the venous system, as measured in these experiments, is probably a later phase in the process than the initial increase of volume, which is used as an index in the plethysmographic methods.

The exact relationship between the results obtained by the plethysmographic methods and the results obtained in these experiments is difficult to state since different units of measurement are employed.

The author concludes that the measurement of the rate of rise in venous pressure in the large veins of the forearm following venous occlusion is at least to some extent, an index of the rate of blood flow in the extremity. Local application of heat to the hand and forearm and exercise of the muscles of the hand and forearm increase the rapidity or rise in venous pressure, while local application of cold decreases it.

HENRIET F. THURGOOD, M.D.

Sherman, R. S.: Varicose Veins; Anatomic Findings and an Operative Procedure Based upon Them. *Ann. Surg.* 1944, 120-172.

A general scheme of arrangement of the saphenous system in the thigh exists but variations are common.

The occurrence of a heretofore unrecognized location of the saphenous vein between the deep fascial layers, of a constant vein perforating the middle of Hunter's canal at about the junction of the upper and middle thirds of the thigh, and of an inconstant perforator vein connecting with the medial genicular venous plexus and the subartorial vein is described.

Although anatomic variations are common, a definite plan exists the surgical significance of this plan is emphasized and suggestions are made for what appears to be more effective operative therapy.

JOHN J. MALONEY, M.D.

Neuhof, H.: The Problem of Embolism of the Pulmonary Artery; Report of a Transcardiac Operation. *Ann. Surg.* 944, 40-452.

The author states that 88 consecutive postmortem examinations at the Mount Sinai Hospital, New York, were studied by himself and a coworker. In this study, obstruction of the pulmonary artery was the essential cause of death in cases of massive pulmonary embolization. The factors producing death were obstruction, asphyxia, and heart failure. In 26 cases, the condition developed during illness and in 62, during surgical postoperative periods. There was evidence at autopsy of previous peripheral embolization in 43 cases.

Some emboli were extremely long, with twiglike branches; others were short and curled up. Some were firm, others friable. A few were firmly adherent. The embolus was situated (1) in the outflow tract of the pulmonary artery (2) in the main trunk and (3) in one or more of the major branches or it was fragmented and distributed in the lesser branches. The author notes that the chances of encountering and removing the embolus at operation cannot be gauged in advance. The symptoms in the 88 cases were those of asphyxia, shock, syncope, or heart failure singly or in various combinations. Although the classical cases can be recognized readily the differential diagnosis from coronary thrombosis, in particular or from noncardiac lesions, in general, may

be difficult or virtually impossible. The electrocardiogram is not of decisive aid.

With regard to the topographic features alone, embolotomy would have been feasible in 33 of the 53 cases. There were no distinctive clinical features to differentiate these cases from less favorable cases. Hence, an operation always must be regarded as an exploratory one. A significant fact concerning the cases to be regarded as favorable for embolotomy was that the duration of life was short in many.

In 1938, there were collected 132 cases in which the Trendelenburg operation had been performed with a mortality rate of 93.2 per cent. Seven patients recovered. The unfavorable features are (1) an extremely high mortality (2) the requirement of a very hasty operation because of the short period of possible occlusion of the pulmonary artery (3) a too formidable operation in case of error in diagnosis, (4) an unsuccessful operation if the embolus is not of classical topography and in the typical situation, (5) the requirement of a specially trained team and (6) the limitation of operation to a rare clinical variety of pulmonary embolism.

One case report is given and the operation used is described in detail. The author states that the operative procedure is simple, reasonably safe and does not require undue haste. Special skill and practice and a special team are not needed. The suction of blood, which results in some measure of decompression of a right ventricle laboring unavailingly against the obstructing embolus is a desirable feature. However, the essential part of the operation is performed blindly and does not provide assurance that suction will engage the thrombus in the eye of the catheter. A metal tube with an appropriately hollowed end would probably be more effective in engaging and extracting the thrombus. Despite the fatal issue in the reported case, further attempts to extract a pulmonary embolus through the right ventricle appear justified. HERBERT F. THURSTON, M.D.

BLOOD TRANSFUSION

Shenkin, H. A. Cheney, R. H. Govons, S. R., Hardy, J. D., Fletcher, A. G., and Starr, I.: On the Diagnosis of Hemorrhage in Man. A Study of Extensive Bleeding in Volunteers. *Am J M Sc* 1944, 708, 421.

It is widely accepted that hemorrhage can be diagnosed by a rapid pulse and a low blood pressure. Because many patients showed none of the signs ordinarily expected after a large hemorrhage the authors are seeking to find by what means this condition can be diagnosed in patients not seen until after hemorrhage has taken place. Furthermore a project of this kind would throw light on the important question of how much blood donors should be asked to give with due regard to their safety.

Eighteen volunteers were bled approximately 500 cc and 17 were bled about a liter. Estimations of the pulse rate, blood pressure, venous pressure, cardiac output (ballistocardiograms) and hematocrit

determinations were made before and after the hemorrhage during the process of recovery and often after replacement of the blood. The technique used is described in detail.

Observations on subjects bled approximately 500 cc showed that in the supine position the average systolic blood pressure diminution was only 9 mm. of mercury immediately after the hemorrhage and there was a slight downward trend for the remaining period of observation. When standing the systolic pressure diminished 14 mm. of mercury after the hemorrhage. In supine subjects the average diastolic blood pressure did not change significantly after the hemorrhage but when the subjects stood, this pressure averaged 7 mm. less after the hemorrhage.

The average pulse rate did not change significantly after a hemorrhage of 500 cc. but when the subject was erect the average increase after hemorrhage was conspicuous and highly significant. This increase was maintained during the period of observation. The average cardiac output and stroke volume changed very little after the 500-cc. hemorrhages. Those were made only in the supine position.

After the subjects were bled approximately 1 liter 11 were observed for about one half hour or less, 5 for three hours and 1 for twenty-four hours before restoration of the blood volume. Hemodilution was followed by means of the hematocrits. In 11 cases samples were taken before and within twenty-five minutes of the cessation of bleeding; in these the reduction of corpuscle volume averaged 2 per cent. A slowly increasing dilution of blood took place after hemorrhage but the blood volume was not restored in any of the cases during the period of observation. Observations made of the blood pressure while the subjects were recumbent showed that after the minimum had passed the blood pressure increased slowly. If first seen two hours after the event the hemorrhage would never have been suspected from the blood pressure readings which were taken while the subjects lay at rest.

The pulse rate after these large hemorrhages exceeded 100 in no case except that of the subject who had had a corresponding tachycardia before the event. Slowing of the pulse was more common than acceleration. In subjects first seen after the event the authors noted that the hemorrhage could never have been diagnosed from the pulse rate. The venous pressure was estimated in 7 subjects. There was either a small diminution or no change after hemorrhage. In the absence of acute attacks the estimations of cardiac output would have provided no clear evidence of the preceding blood loss in the great majority of instances.

When the subject arose after a large hemorrhage, he could not tolerate the erect position because of faintness and dizziness and these were soon followed by collapse if he was not immediately laid flat. Two subjects bled smaller amounts in proportion were able to stand without collapse but the abnormal increase in their pulse rates on arising indicated the strain to which the circulation was sub-

jected. The acute symptoms which so many subjects experienced when they stood upright and a few when they lay recumbent, differed only in their severity. In 2 subjects who did not faint on arising, the systolic blood pressure which normally changed 5 mm. on arising fell from 10 to 30 mm. of mercury. In the 4 who became faint, the blood pressure tended to collapse as the symptoms appeared. Diastolic pressure in either position was not greatly affected.

The effect of hemorrhage on healthy men may be divided into three stages of severity. In the first stage the subject is symptom free at rest and has a pulse rate and blood pressure within normal limits, however when he arises an undue acceleration of pulse rate and some diminution of blood pressure are found. In the second stage there are still no noteworthy abnormalities as long as the subject is recumbent and at rest, but the upright position cannot be tolerated and syncope soon overwhelms him if he arises. In the third stage syncope attacks accompanied by bradycardia occur even though the subject is at rest and recumbent. These attacks seem to be of physiological and not of emotional origin.

The old concept that acute hemorrhage can be readily diagnosed by a rapid pulse and a low blood pressure is erroneous. Three things have probably contributed to the traditional viewpoint. First, a rapid pulse and low blood pressure are characteristic of rapid hemorrhage in anesthetized animals. The fact that the unanesthetized animal can stand a much larger loss of blood without undue acceleration of the pulse and diminution of blood pressure is not so widely known to clinicians. Second few clinicians have ever seen a hemorrhage in which they had any exact idea of the amount of blood lost, and so they were not in a position to criticize the common view. Third in many hospital cases hemorrhage is associated with trauma, and it is beyond dispute that rapid pulse rate and low blood pressure may be associated with shock.

Recumbent subjects may be bled to the point of collapse without exhibiting conspicuous tachycardia, and during the period of severe symptoms profound bradycardia is the rule. The blood pressure usually remains within the normal range until the symptoms of collapse begin, when it diminishes profoundly. Hemorrhages causing no signs or symptoms as long as the subjects are recumbent can be detected by having them sit or stand upright, then the symptoms described will speedily betray the abnormality.

HENRIET F. THURSTON, M.D.

Denstedt, O. F., Osborne, D. E., Stansfield, H. and Rochlin, I.: The Survival of Preserved Red Cells after Transfusion. *Anesthesiology* 944.

5 37

Fantus' idea of the blood bank in 1937 gave a tremendous impetus to the use of preserved blood. The use of preserved blood may well be regarded as one of the most important advances in medicine.

In the storage of whole blood the primary concern is the preservation of the erythrocyte. This implies

not only keeping the cell membrane intact, but also retarding the autolytic changes within the cell which impair its functional properties when it is again placed into the circulation. While the integrity of the cell membrane may be influenced by many agencies directly as for example by the action of hemolytic agents either present in or added to the blood it is now realized that hemolysis during storage is brought about largely as a result of autolytic changes within the cell. As soon as blood is removed from the body the cell membrane undergoes marked changes in permeability especially in the cold. Potassium ions diffuse out of the cell while sodium ions enter from the plasma. Complex organic phosphates in the cell undergo autolytic hydrolysis with the liberation of phosphate. Glucose breaks down to lactic acid and other intermediates. Some of the products of autolysis, including phosphate, do not pass through the membrane readily at lower temperatures. Hence as the osmotic pressure gradually increases, water enters the cell which causes it to swell and ultimately to burst.

Individual bloods differ in regard to cell stability, i.e., rate of hemolysis during storage and preservative solutions may differ greatly in their cell stabilizing qualities. Sodium-citrate solution alone although still fairly widely used, is among the poorest of preservatives. In this solution hemolysis usually becomes visible after about the fifth day and the majority of the red cells undergo irreversible changes by the tenth day. The addition of dextrose to citrate, on the other hand, greatly improves its preservative qualities. In isotonic citrate-dextrose the rates of autolytic change and of cell swelling are much reduced. Blood may be kept in this mixture for six weeks and sometimes for two months with negligible breakdown of cells. The stability of the red cells is influenced also by the proportion of diluent used. With isotonic citrate-dextrose the maximum stability appears to be obtained with most bloods in the dilution of one volume of blood to one half volume of diluent. In phosphate-buffered citrate-dextrose blood may be diluted much further and may be stored at higher temperature, e.g., at 8° or 10° C., without impairment of the stability of the cell.

Since there is no in vitro test for the vital capacity of red cells the only means of testing the influence of storage and of preservative mixtures is to transfuse the cells and follow their survival in the recipient.

The survival of erythrocytes after transfusion has been variously estimated as from thirty to eighty days, depending on the method employed. Some may remain in the circulation for one hundred and thirty days or even longer.

Cell survival is greatly prolonged when preservative mixtures containing dextrose are employed. Dextrose appears not only to stabilize the cell membrane but also to retard autolytic changes during storage, hence it may be considered a true preservative.

To test the merits of two preservative mixtures, i.e., a modified DeGowin's citrate-dextrose, and a buffered citrate-dextrose 35 transfusions were per-

formed, with bloods ranging from strictly fresh to samples stored up to fifty-seven days. All subjects were serologically negative and were in good health from a nutritional point of view. The cell survival was studied by Wiener's method.

Both the buffered and the unbuffered preservative mixtures used in this study give very satisfactory preservation of the erythrocytes. The buffered solution tends to reduce the packing of cells on sedimentation and hence facilitates resuspension. It also is the more effective in retarding autolytic changes during storage, notably the breakdown of labile organic phosphate compounds. Despite these merits however the red-cell survival after transfusion was not noticeably superior with the buffered solutions. While some bloods keep better than others, cells stored up to eighteen days may be considered equivalent to fresh cells, as a rule. No toxicity develops in blood stored up to two months, i.e. long after the majority of the cells have lost their functional qualities.

The relatively rapid disappearance of other elements, such as white cells, platelets, prothrombin, complement and hemopoietic properties from blood during storage presents no serious problem since when fresh blood is required it is usually obtainable from the blood bank. For secondary anemias and especially in acute hemorrhage blood stored for three weeks and even longer is efficacious. Under war conditions, and particularly in areas within bombing range, it is necessary to maintain large supplies of blood and plasma. While it is desirable to keep within the three-week storage limit, there should be no hesitation in using specimens up to a month old in emergencies. Numerous instances have been reported in the present war in which month-old blood has been used with good results.

Under the conditions of the present study red cells can be stored for six weeks and in some instances two months with less than 1 per cent hemolysis.

STEPHEN A. ZIEGLER, M.D.

Janeway C. A.: Clinical Use of Products of Human Plasma Fractionation. Albumin in Shock and Hypoproteinemia; Gamma Globulin in Measles. *J. Am. M. Ass.* 1944, 126: 674.

By the application of large scale methods of fractionation (developed in the Department of Physical Chemistry of the Harvard Medical School Boston) to pooled human plasma from blood collected by the American Red Cross concentrated human serum albumin gamma globulin antibodies isohemagglutinins, fibrin films, and fibrin foam with thrombin have been made available for clinical use.

Concentrated human serum albumin as dispensed in the standard Army and Navy package provides a compact, stable solution which is ready for immediate use in the emergency treatment of shock.

The use of albumin in cases of shock due to hemorrhage, trauma and burns results in an increase in blood volume, hemodilution and clinical improvement. The blood volume is increased in these conditions by approximately the amount to be expected

from measurements of its osmotic pressure (18 cc. per gram of albumin).

In the presence of severe dehydration albumin must be supplemented with fluids in order to obtain the maximum therapeutic effect.

Albumin is an extremely safe blood derivative and it can be administered very rapidly without reaction even after periods of heating at temperatures of 50 C. for as long as one hundred days.

Albumin can be used to correct hypoproteinemia if sufficiently large amounts are used.

In the nephritic syndrome the injection of albumin is followed by a definite increase in proteinuria but does not regularly result in a diuresis.

Gamma globulin antibodies (fraction II of Cohn Strong, Oncley, Hughes and Armstrong) contain most of the antibodies of pooled normal human plasma in 15 fold concentration over the original plasma. Gamma globulin antibodies are the safest and most effective agent available for the prevention and modification of measles by passive immunization. For this purpose the injection should be given preferably on the fifth day after exposure. At this time a dose of from 0.1 to 0.075 cc. per pound will completely protect most susceptible individuals while one of from 0.015 to 0.02 cc. per pound will result in mild measles in most cases. The mild measles in patients receiving globulin is similar to that previously observed in patients immunized with convalescent serum or placental extract. Complications were noted in 3 of 400 cases of measles in immunized children but it occurred in patients in whom the globulin failed to modify the disease. Reactions were noted in only 1.7 per cent of 1,843 intramuscular injections. One half of these consisted of local soreness and most of the remainder of fever. Only one anaphylactoid reaction occurred which was probably due to an idiosyncrasy. Gamma globulin is very effective in controlling the spread and severity of measles in pediatric wards but does not appear to be effective in the control of chickenpox. J. M. MORA, M.D.

Ingraham, F. D. and Bailey, O. T.: Clinical Use of Products of Human Plasma Fractionation: The Use of Products of Fibrinogen and Thrombin in Surgery. *J. Am. M. Ass.* 1944, 126: 680.

The preparation of purified human fibrinogen and thrombin has made possible new materials for use in surgery. The solutions of the proteins may be employed and a variety of products may be prepared by combining them under different conditions. Of these, fibrin foam with thrombin is a new absorbable hemostatic agent prepared from fibrinogen and thrombin of human blood plasma.

Extensive clinical use of fibrin foam with thrombin in neurosurgical operations has shown it to control oozing from the dura from beneath bone flaps and from the cerebral tissues as well as from the dural sinuses and large veins. It is not recommended for brisk arterial hemorrhage.

The tissue reaction to fibrin foam with thrombin is minimal and negligible from the clinical standpoint.

In this respect, as well as in regard to its availability ease of manipulation and adaptability fibrin foam with thrombin is much superior to muscle. It is prepared wholly from materials of human origin.

This hemostatic agent can be used with advantage in certain procedures by the general surgeon. It is also effective in controlling hemorrhage in patients with hemophilia.

A limited use has been made of solutions of fibrinogen and thrombin in certain special situations in which it is desirable to form a clot *in situ*.

Fibrin film is a homogeneous sheet prepared from human fibrinogen and thrombin. It has proved effective in the repair of dural defects and the prevention of meningocerebral adhesions.

J. M. MORA, M.D.

Jacobson, S. D. and Smyth, C. J.: Gelatin as a Substitute for Plasma; Observations on its Administration to Human Beings. *Arch. Int. Med.* 944, 74 254

This study on human subjects was designed to obtain information regarding the value of gelatin as a plasma substitute. Fifty six injections of gelatin were given to 45 subjects in amounts ranging between 450 cc. to 1,000 cc. the rate of injection varying from 56 cc. to 10.2 cc. per minute. Gelatin solution was also given to 3 moribund patients and their tissues were subsequently examined histologically.

The effect of the gelatin solution on the plasma volume was measured in 12 subjects. The immediate average increase in plasma volume was found to be 58 per cent of the volume of gelatin solution administered after four hours it was 70 per cent and after twenty four hours 46 per cent. The disappearance of gelatin from the blood stream was studied in 12 patients and the amount recovered in the urine of 8 of these patients was measured. The blood-stream concentration of gelatin decreased progressively from an initial value of 0.6 gm. per 100 cc. to less than 0.1 gm. in twenty four hours. Throughout the period studied the elimination of gelatin proceeded at a more rapid rate than the fall in plasma volume, 87 per cent of the gelatin having disappeared from the blood stream in twenty four hours while the average plasma volume increase at this time was 46 per cent of the volume of the gelatin solution injected. Approximately 46 per cent of the gelatin injected was recovered from the urine in the first four hours and an additional 30 per cent was recovered in the next twenty hours. The excretion of gelatin in the second twenty four hour period was

slight so that the average total amount recovered in forty-eight hours was 81.3 per cent of the amount injected.

No significant changes in the levels of blood urea nitrogen and amino acids were found during the period of observation. The increase in erythrocyte sedimentation rate was uniformly marked and was found to parallel the gelatin concentration in the serum, being approximately normal at the end of twenty four hours. In 3 moribund patients who received repeated injections of gelatin and whose tissues were later examined histologically no pathological changes were noted which might be attributed to the gelatin, nor was any evidence observed of retention of the gelatin in the tissues. Elevation of the blood pressure and clinical improvement were observed in each of 50 patients who were given gelatin solution for shock therapy. No untoward reactions were observed during or following any of the infusions.

JOHN L. LOMQUIST, M.D.

RETICULOENDOTHELIAL SYSTEM

Bersack, S. R.: Hodgkin's Disease. *J. Am. Med. Ass.* 944 26 025

The patient who is the subject of this report was encountered in a study of 353 cases of Hodgkin's disease. The unusual features of this case and the rarity of cutaneous Hodgkin's disease are deemed sufficient justification for the publication of this report.

The case of cutaneous Hodgkin's disease reported illustrates a rapid terminal spread through the blood stream and the additional unusual feature of ulceration of the Hodgkin's skin lesions. The fact that no malignant cell could be found in the microscopic examination of the early skin nodules caused by blood-stream spread is in favor of a virus etiology of Hodgkin's disease. The hematogenous dissemination must have been mediated through the humoral content of the blood. The only alternative would be to incriminate the few lymphocytes found in the initial stage of a new focus. They might possibly be the vectors of the virus.

The theory of a virus etiology of Hodgkin's disease is an attractive one in that it will explain the early clinical features of an inflammatory nature and also the later development into a seemingly autonomous neoplastic disease. This theory deserves further clinical and experimental study. It may be worth while to attempt transmission experiments with blood derived from a patient who as in the present instance, is exhibiting blood-stream spread.

JOHN E. KIRKPATRICK, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Bell, R. C.: Analysis of 259 Flying Bomb Casualties. *Brit. M. J.* 1944, 2: 689

This report relates the experiences of a small emergency hospital during the flying bomb raids on Britain. During this bombing period, 222 casualties on an out-patient basis and 259 in patients were treated. The greatest number of casualties on one admission reached 26 and of these 12 had to be taken to the operating room. Injuries due to flying glass occurred most frequently and exceeded more than half of the total number of casualties. Most of these injuries were above the nipple and usually caused severe damage to the face, neck or eyes. In 10 cases the globe of the eye was completely destroyed. Flying glass rarely pierced the deep fascia but usually lay in hundreds of small pieces under the skin and subcutaneous fat.

Early careful surgical toilet of these wounds under anesthesia seems to be contraindicated especially if debridement lasts for more than one hour. It is recommended that this type of casualty be permitted to recuperate thoroughly from shock before surgery is begun. Penetrating wounds from bomb splinters were few because the fragments were small, the coefficient of friction high and the velocity low. On rare occasions the bomb fragments were large, and in these instances severe surgical damage was produced. Masonry injuries became more common when people learned to take cover. However the crush syndrome with edema of the injured part, anuria, and uremia was not encountered, because of the increased speed and efficiency of the rescue squads. Blast injuries affecting the lungs were manifested by pain in the chest, dyspnea, and bloody sputum. Blast injuries of the eyes caused a variety of effects, from a feeling of pressure and smarting in the eyes to perforation of the globe, hyphema, and subconjunctival hemorrhage. Blast injuries of the head were usually of the cerebral concussion variety. Burns from flying bombs were

TABLE I.—MASONRY INJURIES (52 CASES)

Description	No. and remarks	Deaths
Fractures of limbs and pelvis	23 (6 severe; 7 minor) T	3
Fractures of skull	7	6
Dislocations:		
Hips		
Thumbs		
Shoulder	T	
Long injury	(with surgical emphysema and hemoptysis)	
Braking	7 3 T	

TABLE II.—BLAST INJURIES (26 CASES)

Description	No.	Remarks	Deaths
Eyes:			
Hyphema	4		
Injured iris			
Subconjunctival hemorrhage	3		
Conjunctivae			
Lungs	6	T	
Cerebral concussion	4		
Cerebral contusion	3	Two cases had blood in C.S.F. One had free blood cells in brain tissue (see above). One had sudden paralysis of left arm	
Severe bruising			

few in number and these were treated by accepted methods.

Nonsurgical injuries from flying bombs caused a variety of pathological states. Hysteria and fear often created a condition of "psychological shock" which required rest and reassurance. These pa-

TABLE III.—HEAD INJURIES (23 CASES)

Agent	No. and description	Deaths
Masonry	7 cranial fractures	6
	cerebral irritation (blood in C.S.F.)	
	unconscious	
Blast	paralysis of left arm	
	partial paralysis of left arm	
	mental confusion	
	3 contusions	
	4 concussions	
Cases unknown	unconscious	1
	contusion	
	concussed (4 hours retrograde amnesia)	
Bomb splinter	lodged in frontal lobe (now convalescent)	

TABLE IV.—FRACTURES (39 CASES)

Agent	No. and description	Deaths
Masonry	23 (mostly severe fractures), T	3
Glass	4 palm fractures	
Bomb fragments	5 severe	1
	3 palm	
Cases unknown	4	

The dosage varies considerably with each patient. The authors recommend a first injection of 0.5 mgm. per pound of body weight, less 30 mgm. and increase of each injection by 10 mgm. Each injection should be prolonged for a period of from one to one and one half minutes. It is advisable that the full two-minute period elapse between additional injections.

Finally curare is to be used with caution prior to endoscopy in patients with a marked diminution in tidal exchange. Cyanosis with convulsions occurred in 3 cases of this type, while difficulty in breathing manifested itself in 2 additional cases of this type.

Curare relaxes the striated musculature and may be useful in troublesome endoscopies. On the other hand since it is difficult to determine the exact dosage for each patient and since the effects of the drug are so unpredictable, curare may not be used for endoscopy with safety. To obtain relaxation for endoscopic procedures other measures are preferred, such as adequate preoperative medication with the barbiturates by mouth and with morphine and atropine by subcutaneous or intravenous injection or the intravenous use of barbiturates.

The curare preparation used in this report is marketed under the name "Intocostin."

BENJAMIN GOLDMAN, M.D.

Felmus, L. B., Woods, C. C., and Spreng, D. H., J.: Pilonidal Cysts. *Arch. Surg.* 1944, 49: 316.

Various theories concerning the cause of pilonidal cysts are discussed as well as the high rate of delayed healing and the recurrence of pilonidal infection following operation. In view of the fact that recurrence of infection may result from failure to dissect out all the finer ramifications of the sinus, from persistence of infection or bacterial contamination due to the proximity of the anus, from the poor blood supply following the formation of fibrous scar tissue or from a combination of these factors, the authors have succeeded in reducing the rate of recurrence by careful attempts to eliminate all these possible causes.

At the Oliver General Hospital, Augusta, Georgia, (except in cases with the formation of abscesses) the procedure has been excision en bloc, with primary closure of the resulting wound. Prior to operation the patients are instructed to take Sitz baths several times daily. The sacrococcygeal area is prepared the day before and on the day of operation and as little healthy tissue is removed as is consistent with complete excision of the sinuses and cyst. The general direction and depth of the tracts are determined by probing at the onset. The open wound is then irrigated and dusted with sulfanilamide powder. With careful attention to hemostasis and the obliteration of dead spaces, closure is effected with non-absorbable sutures. Undercutting of the skin has rarely been necessary. A point is made of accurate apposition of the cutaneous edges, followed by the release of retained blood from the wound and covering of the wound with a strip of sulfanilamide gauze

TABLE I—RESULTS OF TREATMENT

	Per cent of cases
Healed by primary union	65
Healed by secondary union after primary closure	34
Recurrences	1

The average stay in the hospital, including two weeks of reconditioning, was fifty-one and seven-tenths days.

and a pressure dressing. Stress is placed on cleanliness of the lower part of the back and the avoidance of fecal contamination of the wound.

In cases of recurrent sinus or persistent infection of an imperfectly healed wound, reoperation is performed exactly as outlined and as often as deemed necessary after a few weeks and after the usual cleansing Sitz baths.

The table above summarizes the results in the first 100 patients so treated.

Only 2 patients of the 54 who were admitted to the hospital without previous operation had recurrences. Follow-up inquiries indicate that about 5 per cent have been rehospitalized after discharge from the hospital. The authors believe that the problem of pilonidal cysts and their delayed healing is one of infection and of wound healing rather than of true recurrence of the pilonidal sinuses.

JOHN L. LINDEQUIST, M.D.

Graham, D. P.: Rapid Replacement of Fluid in Hemorrhage and Shock. *Brit. M. J.* 1944, 2: 633.

Many authors are of the opinion that the rapid introduction of fluids into the circulatory system of the body causes acute dilatation of the right side of the heart. In a series of battle casualties in the Mediterranean theater of war fluids were infused rapidly and observations were made of any ill effects which this procedure might have on the heart and circulation in the lungs. The patients were received from on half hour to twenty two hours after being wounded. All were suffering from physical fatigue, a degree of anxiety neurosis, dehydration, and from the effects of severe trauma and blood loss.

All patients received 3,000 units of antitank serum intramuscularly and 2½ gm. of sulfanilamide by mouth. Routine resuscitation measures were carried out. The fluids were infused under pressure by attaching a Higginson syringe to the air inlet.

Ten case histories are given in detail. The temperature, pulse, respirations, blood pressure, hemoglobin, and general condition of the patients were checked and the findings were considered typical of those in a larger number of patients treated.

In cases in which the blood loss is estimated to be severe (about 2 liters) replacement cannot be too speedy. It is estimated that the patients in this series lost an average of 54 liters of blood. The incidence of reactions was less than in cases in which fluid was given slowly and in small quantities. When sufficient time had elapsed to allow the hemoglobin to fall considerably there were no signs of overloading of the circulation. In cases in which there was

embarrassment of the cardiovascular system as a result of toxemia damage to the thoracic contents or continued internal hemorrhage rapid transfusion was harmful. Cases of trauma to the limbs, with gross hemorrhage showed an excellent response to this rapid technique.

The points of contrast between shock and the effects of hemorrhage are so numerous that the assumed identity of these conditions is no longer defended.

The case histories showed that these patients suffered mainly from posthemorrhagic hypotension combined with a certain degree of shock. If the shock is not too profound the heart is capable of dealing adequately with large volumes of infused fluid and the vascular bed is capable of retaining this added fluid for use by the circulation.

Infusions at the rate of 143 cc. a minute in no way embarrassed the cardiac mechanism. Patients with toxemia (peritonitis) and wounds of the lung developed pulmonary edema after mass infusion. Patients with peripheral trauma and hemorrhage without sepsis did not develop pulmonary edema.

The author recommends that an estimate be made of the loss of blood volume in the battle casualties who require blood transfusion. Hemoglobin readings should be made before and after the infusion of plasma. The estimated loss of fluid should be replaced rapidly with the aid of pressure to prevent the development of post traumatic hypotension into true shock.

RICHARD J. BENNETT JR., M.D.

Guthrie, D. and Schimmel I: Drainage in Thyroidectomy *Surgery* 1944, 16 725

The necessity of drainage after thyroidectomy seems to depend on the kind of suture material used. All of the wounds sutured with catgut had to be drained, while 82 per cent of those sutured with silk could be closed. However since the use of cotton the authors have drained only 8 of 580 thyroidectomy wounds.

All the drains are placed under the skin flaps and not in the goiter bed. The wound is closed with clips and No. 80 cotton is used on the skin flap. All dissection must be sharp. The authors suture the sternothyroid muscle in the midline and if necessary, to the base of the remnant. To prevent flap oozing they employ a special notched rubber sponge over the flap. The details of the technique should be read in the original article.

FRED S. MODERER, M.D.

Kraybill, W. G.: Total Disruption of Surgical Wounds of the Abdominal Wall, with Reference to Plasma Proteinemia and Plasma Ascorbic Acid. *Am. J. Surg.* 1944, 66 220.

The disruption of abdominal wounds is a distressing complication of abdominal surgery. Investigation has emphasized the importance of the protein metabolism and the role of vitamin C in wound healing. The deleterious influence of foreign bodies in the form of reactive suture material has also been established clinically and experimentally.

In a series of 375 cases of abdominal section there were 7 (1.8 per cent) with total disruption of the wound. These were studied with special reference to proteinemia, detectable ascorbic acid in the plasma and the fate of the catgut sutures.

In 6 of the 7 cases the plasma protein was below the lower limit of normal—6.5 mgm. per cent, only 1 patient had this level. In none of the cases was there detectable ascorbic acid in the plasma at the time of total disruption. In 5 cases the administration of 150 mgm. of ascorbic acid a day was inadequate to produce a detectable quantity in the plasma within a week.

It has been established that reactive suture material plays an inhibitory role in wound healing. Wire has been shown to give the least reaction, while cotton silk, plastigut, nylon and catgut show increasing reactivity in the order given.

In addition to the diminution of plasma protein and ascorbic acid, the disrupting forces of coughing and excessive distention are probably contributing factors. In this series the factors of age, carcinoma type of incision, drainage through the wound, infection and general nutrition were also unquestionably contributory to the total abdominal wound disruption.

SAMUEL KAHN, M.D.

Helfrick, F. W. and Abelson, N. M.: Intravenous Feeding of a Complete Diet in a Child. *J. Pediatr.* S. Louis, 1944 25 400.

A five-month-old white infant with Hirschsprung's disease, complicated by a digestive upset and upper respiratory infection developed a most extreme picture of marasmus which gave every indication of an impending fatal termination. The baby was given a complete intravenous feeding for five days with fats, carbohydrate and amino acids in proportions and quantities recommended in a normal infant's diet. There was a prompt dramatic improvement in the nutrition which permitted eventual successful treatment of the Hirschsprung's disease with proctigmine. This is the first case on record of complete feeding by vein alone for a significant period of time.

The details of the intravenous feeding were as follows:

The preparations available for intravenous administration were 50 per cent glucose solution, a 10 per cent solution of amino acids (amigen) and a 10 per cent emulsion of fat. The fat emulsion consisted of olive oil and lecithin in a 2:1 ratio suspended in water the total lipid concentration being 10 per cent. This material was passed through a dairy homogenizer and was subsequently given sixty minutes of irradiation to cause further dispersion of the fat particles.

The parenteral feeding was designed to provide 58 per cent of the calories (300 calories) from carbohydrate, 12 per cent (60 calories) from amino acids and 30 per cent (160 calories) from fat. This required the daily administration of 150 cc. of 50 per cent glucose solution, 150 cc. of 10 per cent amino acids and 180 cc. of 10 per cent fat emulsion. An

additional 120 cc. of normal saline solution was given, to make a total fluid intake of 600 cc. per day.

To administer these preparations a continuous intravenous drip apparatus was used. A 20-gauge needle with a stylet was tied in place in the left saphenous vein just anterior to the medial malleolus in the left ankle. The remainder of the apparatus consisted of an open-top graduated cylinder, connected by rubber tubing to a Murphy drip and from there to a metal attachment which could be inserted into the needle. The solutions, in the quantities determined were introduced into the apparatus on the following schedule: 12 midnight, 60 cc. of 10 per cent fat emulsion, 3 a.m. a mixture of 50 cc. of 50 per cent glucose, 50 cc. of 10 per cent amino acids and 30 cc. of normal saline solution. At 8 a.m. and at 4 p.m. these solutions were repeated in the same order.

The rate of flow was adjusted so that the administration of one solution was finished at about the time the next one was due, but if any solution ran in completely before the time was up the apparatus was disconnected and the stylet used to close the needle. Later the solutions were permitted to run in faster so that the drip was intentionally interrupted for periods as long as four hours. The use of the stylet permitted the interruption of the infusion at any time, so that the baby could be moved, turned, or weighed, and the apparatus cleaned and sterilized.

The chief purpose in introducing the solutions separately instead of mixing them all together was to avoid having the fat stand for any length of time in contact with saline solution, since solutions of electrolytes neutralize the charge of fat emulsions and cause, in time, some coalescence of the fat particles into larger aggregates.

EDMUND E. ARNHEIM, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Pope, C. H., and Perkins, R. M.: Differences in the Patterns of Bites of Venomous and of Harmless Snakes. *Arch. Surg.* 944, 49 33

The literature on snake poisoning is misleading in stating that a pit viper makes only one or two large punctures when it bites. In contrast to the several rows of small ones made by a harmless snake. The reason for this is said to lie in a difference between the behavior of the two types of snakes. I.e. the pit viper merely stabs with its pair of long fangs, whereas the harmless snake actually bites. It is demonstrated in this article that pit vipers of the United States bite as effectively as most innocuous snakes in no sense do they merely stab. The bite pattern of the pit viper though not simple, can be recognized. Moreover a careful study of the bite may reveal the approximate location of the pocket of venom, the size of the snake, and even its generic identity.

In dealing with any physical injury the first step is to make an exact analysis of it. In the case of snake bite, one must first determine whether one is

treating actual snake poisoning or merely superficial scratches and pricks of a harmless snake. Physicians who report cases of poisoning should include diagrams of all marks made by teeth and fangs and thus help in the accumulation of data on bite patterns. Directions for the treatment of snake bite should explain the true difference between the bite patterns of harmless and venomous snakes and explain how interference by clothing will invariably modify both.

J. M. Moma, M.D.

Converse, J. M., and Robb-Smith, A.H.T.: The Healing of Surface Cutaneous Wounds: Its Analogy with the Healing of Superficial Burns. *Ann. Surg.* 1044, 120 873.

Interest in the healing of cutaneous wounds produced by the removal of skin grafts was aroused by the fact that the wounds of superficial burns appeared to present a similar process of healing. Brown and McDowell made the same observation, and later Cannon and Cope used skin graft donor areas to test the effect of coagulants on epithelial growth.

Four hundred and sixty nine skin-graft donor areas were studied. These skin grafts were removed for use in plastic operations and for the covering of raw areas created by burns or trauma. Three types of skin grafts were employed: thin Thiersch grafts, thicker split (intermediate) grafts which were removed with the Blair skin graft knife and skin grafts of varying thickness (from 0.010 to 0.042 inches) cut with Padgett's dermatome. The donor sites used were the medial aspect of the arm, the abdomen, the back, and the thigh. A few grafts were removed from other regions of the body.

The routine postoperative treatment of the donor areas was as follows: gauze soaked in 1/1000 adrenalin solution and large saline packs were held with pressure against the bleeding donor area. Then strips of fine-meshed vaselined gauze impregnated with sulfanilamide powder were applied to the wound and covered with gauze, cotton and a pressure bandage firmly anchored with adhesive. The dressings over the skin-graft donor areas were removed when the latter were healed. The approximate healing time of these donor areas was observed the dressing being removed when the vaselined gauze could be easily detached from the new epithelial surface.

It is obvious that accurate comparative data are difficult to obtain because the thickness of the graft, which is cut with the dermatome, varies greatly with the thickness of the cement which is employed to produce adherence of the skin to the dermatome drum, because of individual variations in the characteristics of the skin of the different patients, and because of variations of the age and general condition of the patients. However it is believed that observations in a sufficient number of cases (469) have permitted the following conclusions:

In the study of superficial burns, a comparative study of 500 donor areas of partial-thickness skin grafts was made. The following facts were noted:

1. The quality of the repair was roughly proportional to the rapidity of healing

2. The rapidity of healing was dependent upon (a) the thickness of the graft removed (Thiersch from six to ten days intermediate, fourteen days full-thickness, from twenty-one to fifty-eight days), (b) the thickness of the skin of the donor site and (c) the presence or absence of infection

3. Epithelial healing originates from the epithelial elements in the dermis, hair follicles sebaceous glands, and sweat ducts. The number of these elements decreases in the depth of the dermis and so healing is slow

4. In slow healing areas abnormal fibrous tissue is laid down in excessive amounts. The epithelium formed is of poor quality

5. Contraction following healing is appreciable in areas from which grafts have been cut near the base of the dermis. In deep dermal burns and in mixed burns, such a contraction has been observed and is called "interland contraction"

From 101 burned patients, 63 biopsy specimens were removed. The extent of the anatomic destruction of the burn wounds and the mode of healing of these wounds were observed.

An anatomic classification of burns is proposed.

A description of the clinical and pathological aspects of superficial burns is given

The authors point out that there may be need for skin grafting in certain superficial burns particularly on the dorsum of the hand and around the joints in ectropion of the lids in distortion of the features of the face because of tightness produced by interland contraction, or because of poor quality of the healed skin.

JOHN E. KIRKPATRICK, M.D.

Feinman, M. H.: Tropical Ulcer. *N. Eng. J. M.* 1944, 331: 578

Feinman presents a clinical discussion of the disease variously known as *ulcus tropicus*, tropical sloughing phagedena, and Naga sore. It consists of an acute or chronic skin lesion of uncertain etiology but closely related to the presence of spirochetes and fusiform bacilli, and characterized by an irregular or rounded appearance indurated edges an excavated base, a dirty greenish-gray sloughing membrane and red granulation tissue in the base and walls. These ulcers usually occur on broken or injured skin. Therefore, all troops should be cautioned about this so that they may promptly apply a bactericide and first-aid dressing in an effort to prevent ulcer formation at these points.

Medical officers should learn to recognize these ulcers early. They should not experiment with the easily available sulfonamide drugs or ointments, gentian violet or Frazier's solution to see what will happen but should proceed directly to treat them vigorously with the intravenous injection of mapharsen and the local application of sulfanilamide or sulfadiazine powder as their appearance or bacteriology may direct. After the ulcers have become

clean occlusive vaseline dressings should be applied and changed infrequently

Mapharsen can and should be made easily available to forward echelons and treatment should be instituted in the early stages of the ulcer. In this way patients can remain ambulatory, with no loss of work or fighting and no hospitalization.

J. M. MORA, M.D.

Southworth, J. L.: The Effects of Sulfanilamide Locally Implanted in Clean Wounds. *Am. J. Surg.* 1944, 66: 345

A study was undertaken to determine the effect of local sulfanilamide implantation in clean wounds. Patients with bilateral inguinal hernias were selected as subjects. Through 2 separate inguinal incisions a routine bilateral hernioplasty was performed at one sitting. The layers were sewed with interrupted catgut stitches. Sulfanilamide powder was placed in one side and omitted in the other. Five grams of the drug were used; they were spread evenly throughout the layers of the wound. In 11 patients unsterile crystalline sulfanilamide was used and in 14 sterile drug was employed. To obtain further controls no drug was used on either side in 12 cases.

Careful observation of these cases leads to the conclusion that sulfanilamide in hernioplasty wounds frequently produces hemorrhage into the wound and surrounding tissues and sometimes produces an increased induration of the wound but it has no effect on healing as determined by physical examination

SAMUEL KAHN, M.D.

Pressman, R. S., and Bender, I. B.: The Effect of Sulfonamide Compounds on Transient Bacteriemia Following the Extraction of Teeth. *Sulfanilamide. Arch. Int. M.,* 1944, 74: 346.

In 30 control subjects and 30 sulfonamide treated patients cultures taken immediately after the extraction of teeth were positive for bacteriemia in 83.3 per cent and 76.7 per cent, respectively. Cultures made ten minutes after the extractions (of from 3 to 10 teeth) showed a more significant difference—13.3 per cent positive for the treated group as compared with 33.3 per cent for the control group.

The bacteriostasis produced by sulfanilamide appears to have not only a delayed quantitative but also an immediate qualitative effect. Aerobically sulfanilamide in vitro exerts no bacteriostasis but, anaerobically it has a marked bacteriostatic effect. Since the organisms circulating in the blood stream are few a sensitive medium must be used to detect their presence.

WALTER H. NADLER, M.D.

Welch, H., Putnam, L. E., Randall, W. A., and Herwick, R. P.: Penicillin. *N. J. Am. M. Ass.* 1944, 126: 1024.

In a recent issue of *Science* it was reported that gonorrhea had been successfully treated with single injections of 100,000 units of commercial penicillin incorporated in a beeswax peanut oil base. The authors have had an opportunity to investigate the

properties of so-called penicillin X sometimes referred to as factor X, or allopenicillin.

Preliminary studies indicate that penicillin X is three to five times more effective than commercial penicillin in protecting mice against 10,000-unit lethal doses of pneumococcus type I.

On the basis of the increased activity of this new preparation against certain organisms in comparison with commercial penicillin it appeared desirable to determine the effect of this preparation on the gonococcus. Accordingly 68 patients with gonorrhea most of whom were sulfonamide-resistant, were treated with a single intramuscular injection of 25,000 units of penicillin X. The group consisted of 35 males and 33 females. Approximately 94 per cent of those treated were cured.

For comparative purposes a group of 31 males and 27 females were treated with a single intramuscular injection of 25,000 units of commercial penicillin. Based on the same criterion 37 patients, or approximately 63 per cent, of those treated were cured.

It is of interest that 3 of the patients not cured with commercial penicillin were cured by a subsequent single injection of 25,000 units of penicillin X.

Although the number of cases reported is small, it further work substantiates the fact that a large proportion of cases of gonorrhea can be cured with a single intramuscular injection of penicillin X, the public health control of this disease, which has been maternally affected by the use of commercial penicillin will be further facilitated.

JOHN E. KIRKPATRICK, M.D.

Peck, F. B. Penicillin; with Special Reference to Its Use in Infections Complicating Diabetes. *Am J M Sc.* 1944, 208 58

The efficacy of penicillin in the treatment of certain types of pyogenic infections together with its remarkable lack of toxicity suggested that the drug might be particularly useful in the management of some of the more localized and generalized coccic infections so frequently encountered in association with diabetes mellitus.

In contrast to the sulfonamides which have been ineffective in the local infections, penicillin is remarkably efficacious. It cannot be expected to restore dead tissue, but it appears of especial value in the infectious type of gangrene when the circulation is intact. In carbuncles and other infections caused by staphylococci results have been particularly striking.

The author employed penicillin locally in 15 cases of diabetes complicated by infection and obtained a rapid and sometimes dramatic response in some of the early cases of carbuncle following the injection of penicillin directly into the infected tissues. The solutions used for this purpose have ranged from 100 to 1,000 per cubic centimeter of saline solution. In no instance has he observed any tendency toward a deleterious effect on carbohydrate tolerance, nor has penicillin administration necessitated larger doses of insulin. The presence of infection notoriously in-

creases the insulin requirement of the diabetic, but in none of the cases described was there any unusual difficulty the patients responding particularly well.

Use of penicillin does not relieve the clinician of the necessity of taking all the other precautions necessary for proper treatment of infections. Drainage must be established surgically since the mere administration of penicillin not only is wasteful but may not be adequate. It is essential to determine the causative organism.

JOSEPH K. NARAY, M.D.

Sophian, L. H.: The Use of Penicillin in Topical Application. *Am J M Sc.* 1944, 208 577

Because of the shortage of penicillin a technique for the extraction of penicillin from the urine of patients under treatment for syphilis, gonorrhea, and septic infections was developed by the author. It was found practical and inexpensive and it yielded from 30 to 40 per cent of the antibiotic substance administered. A considerable number of animal and clinical trials demonstrated that the reclaimed penicillin was nontoxic and nonpyrogenic when used parenterally. Dosages as high as 2,000,000 units a week were administered intramuscularly with excellent clinical results, which differed in no way from therapy with commercial penicillin.

The availability of the material has encouraged the author to make certain observations concerning the use and desirability of topical applications. When consideration is given to the difficulty and expense of maintaining over a period of many days or weeks a high penicillin concentration by parenteral administration topical applications, when practicable, offer a suitable alternative. The author found it possible to reach local levels of penicillin activity by topical administration far in excess of the highest ranges he has maintained by intravenous and intramuscular use, namely between 0.7 and 0.9 units per cubic centimeter of blood, achieved by continuous introduction at the rate of 20,000 units per hour. There are many bacteria including some strains of staphylococci, which are resistant to low penicillin concentrations or even to the high levels noted, but they are susceptible at still higher levels. For the control of such infections, penicillin may be applied topically or by both parenteral and topical routes.

Penicillin incorporated in a suitable ointment, together with a wetting agent, penetrates agar sufficiently to cause inhibition of the bacillus subtilis at a depth of 16 mm. Although it does not demonstrably penetrate through a skin layer in vitro, penicillin in such an ointment base has strikingly effective value in acute and chronic pyogenic infections of the skin and subcutaneous tissues, particularly in syccosis barbae, infected superficial wounds, and furunculosis.

The appearance of a zone of infection under treatment with the ointment is characterized by hyperemia and arrest of suppuration. In an uncomplicated situation like a furuncle the first change is seen after twenty-four hours in a lessening of the peripheral edema and a reduction in tension of the lesion.

Early furuncles resolve in from four to six days but suppurating ones will go on to evacuation. Chronic pyogenic infections respond slowly and develop a considerable zone of hyperemia when the ointment is applied for extended periods. The granulation tissue growth is accelerated and the surface becomes engorged.

The author recommends a penicillin ointment in which aerosol serves as a vanishing cream base.

JOSEPH K. NARAT M.D.

Murphy F. D., La Boccetta A. C. and Lockwood, J. S.: The Treatment of Human Anthrax with Penicillin. *J Am M Ass* 1944 136 948.

The authors for the first time used penicillin in the treatment of 3 cases of uncomplicated cutaneous human anthrax without bacteremia. Exceedingly prompt and excellent clinical response was observed in every instance. The 3 cases are briefly reported.

The clinical response was paralleled by the disappearance of the bacillus anthracis from the lesion. It was found that twenty four hours after the administration of 100,000 units of penicillin the smear was still positive and the culture was negative but in forty-eight hours both the smear and culture were negative. In vitro studies of the strain of 1 case revealed the bacillus anthracis to be 100 times less sensitive to penicillin than a strain of the staphylococcus aureus.

It appears from these studies that a total of 100,000 units of penicillin is the minimum effective dose in the uncomplicated case of cutaneous anthrax. At least a total of from 100,000 to 400,000 units at the rate of 100,000 units per twenty four hours should be given to the average adult. Continuous intravenous infusion is probably the most efficient method of administration although intramuscular injections every two or three hours lead to just as good results.

T. LEUCUTIA M.D.

ANESTHESIA

Crooke, A. C. Morris, C. J. O. R., and Bowler R. G.: General Anesthesia in Shock. *Brit M J*, 1944, 2: 683

The high mortality rate from surgery on patients in shock may be ascribed to hemorrhage to the operative manipulations, or to the anesthesia. In the present study the pulse, respiratory rate, blood pressure, plasma volume, hemoglobin and electrocardiogram were observed in a series of 16 patients with normal initial values of these factors. Changes in blood pressure were produced by variations in the depth or type of anesthesia but were not found to be related to surgical manipulation. Changes in blood pressure occurred independently of any change in plasma volume and hemoglobin level. Changes in blood pressure were not reflected in alterations in the serial electrocardiograms. Cardiographic irregularities were never constant.

Patients in traumatic shock with significant alterations in plasma volume suffered a marked fall in

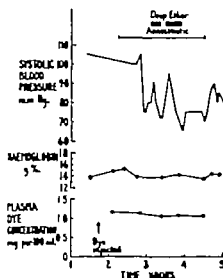


Fig. 1 Effect of nitrous oxide, oxygen, and ether on blood pressure, hemoglobin and dye concentration.

blood pressure due to the anesthetic. Ether or ether and chloroform caused the most profound fall. Sodium pentothal acted in a manner similar to ether. However cyclopropane and oxygen usually increased the blood pressure except in the severely shocked patient.

B. G. P. SHATTUCK M.D.

Lull C. B. and Hingson R. A.: An Evaluation of Continuous Caudal Analgesia. *N York State J M* 1944, 44: 3337

The authors of this article attempt to give the medical profession an unbiased opinion of the value of continuous caudal analgesia for the relief of pain. Team work between the anesthetist and the obstetrician is essential for the proper accomplishment of the technique. The physiology of labor and delivery observed by the midwife and interpreted in our existing textbooks on obstetrics has been completely altered since the inception of successful continuous caudal analgesia. The first stage of labor is dramatically shortened, and the third stage of labor is shortened and simplified so that in many instances hemorrhage in this stage will be unbelievably small. There is a reduction in postdelivery convalescence time with a rapid involution of the uterus, a return of the cervix to its prepregnant state, and a regaining of good muscular tone by the perineum.

Stress was laid on the number of anomalies which were found in the sacra of the 241 cadavers dissected. 22 of all the sacra studied exhibited openings in the roof and more than 11 per cent had a bony defect at the superior pole. Eight per cent had bony defects in the inferior pole. Five tenths, or 1 per cent, of the female sacra and 2 per cent of the male sacra presented no roof at all. In 55 per cent it was found anatomically that caudal needles could not be introduced because of osseous obliteration of the sacral canal. An understanding of the anatomical features involved is important to the successful introduction of a caudal needle. When the sacral

hiatus cannot be felt, the patient is considered unsuited for caudal analgesia. In routine cases however when special medical indications such as tuberculosis or heart disease are presented, these patients are roentgenographed by the Bishop modification of the Moloy technique for a special sacral study. This is considered one of the most important supplementary techniques that have been added to the caudal analgesia technique since its introduction.

Among more than 3,000 personally observed and managed obstetrical patients not a single case was found in which a complete block of the eleventh and twelfth thoracic nerves was not accompanied by the total relief of the abdominal pains of labor. There was not a single case found in which well established contractions of the uterus did not continue if the level of analgesia was not permitted to rise above the tenth thoracic segment. Therefore the authors have confirmed the natural anatomic dissociation between the motor and sensory components and uterine nerves.

Pudendal nerve block can be accomplished by a single caudal dose, which produces a sensory block of the nerve supply to the cervix and eradicates the intense, agonizing crescendo of pain in the lower back.

In from 40 to 60 per cent of the patients there was no significant change in the force, frequency or duration of the pattern of uterine motility under caudal analgesia. The second type of uterine response occurs in from 20 to 35 per cent of the patients and in these there was a constant diminution in uterine tone with increased amplitude of uterine contraction. These labors, like those in the first group, progress rapidly and are terminated successfully. In the third group of patients, the uterine tone may be increased and there is a diminution in the amplitude of the contraction. These responses are frequently associated with a high level of ascent of the analgesia to the point of the fifth or sixth thoracic segment. In these patients the labor pains are ineffectual and the progress of labor is retarded.

It is the consensus of the authors that metycaine (1.5 per cent) though clinically no more toxic than procaine, is definitely more potent. Other reasons are presented for the preference of the former.

The complications associated with this technique were presented, 36,000 deliveries under this method being reviewed.

Researches include the use of continuous caudal analgesia in surgical cases peripheral vasospastic disease, thrombophlebitis, peripheral arterial embolism, scleritis, pruritus ani, and traumatism of the lower extremities. This method has dramatically reduced both systolic and diastolic blood pressures in patients suffering from hypertension. In some patients the reduced blood pressure remained so for as long as two days up to three weeks. This method has given encouraging results in a series of more than 40 eclamptic patients. At the present time the authors are attempting to evaluate the difference, if any, between fractional spinal and continuous

caudal anesthesia. It is their opinion that either one of these methods is eminently satisfactory and that there is very little difference between the two. A group of tables in the article shows the age group, the parity, the presentation of the fetus, the method of delivery, the blood pressure record, and the length of labor in a series of 963 cases. The failures of the method are enumerated, they occurred in 120 patients or 12.5 per cent of the total. Three maternal deaths are listed in this group, none of which is attributed to the use of the continuous caudal analgesia.

The incidence of complications and the contraindications indicate that this is still a technique to be performed by specialists in the hospital.

MARY KARP, M.D.

McClellan, G. S., and Williams, E. L.: Comparative Analysis of Drugs in Continuous Caudal Analgesia. *Am. J. Obst.* 1944, 48, 617.

Pontocaine (0.1 per cent) with epinephrine (1 to 500,000) is a safe and satisfactory caudal analgesic agent. Pontocaine (0.35 per cent) and pontocaine (0.1 per cent) without epinephrine have been unsatisfactory.

Two drugs have been used with equal effectiveness: metycaine and pontocaine. The duration of effective analgesia was of some interest. Metycaine injected in 20-cc. or 30-cc. amounts was effective for between thirty and forty five minutes. Pontocaine (0.35 per cent) injected in the same volume produced analgesia for between forty five minutes and one hour and pontocaine (0.1 per cent) plus epinephrine was effective for as long as one and one-half hours. Caudal analgesia has great possibilities for use in obstetrics and in surgery of the pelvis. It is possible to relieve pains of labor during the first stage and to produce anesthesia for delivery. The baby's respiration is established immediately and no resuscitation is necessary.

The method is one to be used only by persons familiar with local and regional anesthesia and aware of the dangers involved. Caudal analgesia is unsatisfactory for patients with breech presentations.

Since the mechanism of labor is altered with the use of continuous caudal analgesia, no one should attempt to use this method unless he is familiar with the techniques of rotation of the fetal head and the use of the obstetric forceps.

EDWARD L. CORSELL, M.D.

Roman-Vega, D. A., and Adriani, J.: Clinical Experiences with 2-Methyl-Amino-Heptane as a Vasopressor Substance for Spinal Anesthesia: A Preliminary Study. *Current Res. Anesth.* 9:4, 23, 248.

This preliminary report describes an attempt to determine the clinical value of the aliphatic type of vasopressor drugs in spinal anesthesia. It comprises the experience with 2-methyl-amino-heptane in a series of 100 patients undergoing operation under spinal anesthesia.

The drug is a clear colorless volatile liquid which is slightly soluble in water. At the present time it is available only for investigational use and is designated as EA 1 hydrochloride. It causes a rise in both the systolic and diastolic pressures, an increase in pulse pressure, and stimulation of the heart with improvement of its contractions. Dilatation of the pupils, piloerection and other manifestations of sympathetic stimulation, bronchial dilatation and decreased renal volume follow its administration. Its toxicity is low; nausea and vomiting are notably absent.

In each of the 100 cases EA 1 proved to be an effective vasopressor and successfully combated the hypotension of spinal anesthesia. The average effective dose varied between 75 and 100 mgm. When given intramuscularly the effective dose varied from 10 to 50 mgm. It is suggested that if the intravenous route is used, the drug be diluted with saline solution or distilled water (equal parts). In no case did the diastolic pressure fall with the administration of this drug, and in this aspect EA 1 differed from ephedrine. A rise in pulse rate occurred in only 6 per cent of the patients; but 16 per cent had an increase in respiratory rate, 15 per cent had pupillary dilatation which persisted for about thirty minutes, and 5 per cent had nausea and vomiting. There seemed to be excessive capillary bleeding in 3 per cent of the cases. The response was noted within three minutes if the drug was used intramuscularly and within one minute if used intravenously. The drug was felt worthy of further clinical study as a vasopressor substance for combating the hypotension of spinal anesthesia.

MARY KARY M.D.

Holly J. D.: Intravenous Anesthesia in Children.
South. M. J. 1944 37 631

Up to the present time it has been the consensus that pentothal sodium is a poor agent for intravenous use in children: first because of the difficulty of venipuncture, and second, because of the poor tolerance of children to barbiturates. There is no essential difference in the kind of drug given in childhood and in later life, and the question, "When does pediatrics end?" is still a muted problem. A discussion of the drugs used for children demonstrates the similarity of drugs used in the child and to the adult and proves that if drugs are used carefully they can be administered at any age.

The author has found from clinical experience that children tolerate pentothal sodium as well as adults.

The history of intravenous anesthesia is reviewed from the use of chloral hydrate in 1874 to the present administration of barbiturates. The effects of the drug pentothal sodium on the systems of the body are mentioned. A 2.5 per cent solution is prepared and the administration performed by means of equipment consisting of one three-way valve to which is attached a piece of rubber tubing 8 inches long. On the end of the tube is a Luer glass tip to which tip is attached an intravenous needle of 1/4 inch

length and of 22 to 24 gauge, beveled and sharp-pointed.

The veins in the antecubital fossa are usually selected also the wrist veins or the great saphenous vein anterior to the internal malleolus.

Premedication for children up to five years of age consists of atropine sulfate (gr. 1 to 1/50th) given thirty minutes before operation for children over five years of age nembutal (gr. 1 to 1/34) given one hour before operation and atropine sulfate (gr. 1 to 1/50) given thirty minutes before operation.

The technique of administration is described in detail. Fractional amounts of the agent are given as the need for depth presents itself.

Indications for the drug are enumerated and include any type of operation except bronchoscopy. The more severe the illness the greater is the indication for the drug. It can be used in acute shock and hemorrhage. If you can get into a vein you can administer pentothal as an anesthetic agent for the same surgical procedures that are performed in adults. It is contraindicated in inflammations that encroach on the trachea, neck, and posterior pharyngeal wall and in operations that involve the skin only.

There are 2 diagrams of the anesthesia equipment and 12 case records in the original article. The advantages of the drug are summarized and include its rapid induction, comparatively good relaxation, economical use and safety.

MARY KARY M.D.

Large, A. and Heinbecker, P.: Refrigeration in Clinical Surgery. *Ann. Surg.* 1944, 120 707.

The purpose of this article was to discuss the effects of cooling and the effects of asphyxia produced by the application of a tourniquet also to present cases in which a form of treatment was employed which was in harmony with the implications of established physiological principles.

Within physiological limits the velocity of most biological processes varies directly with the temperature. Cellular activity almost completely stops at temperatures close to freezing and the conduction in a nerve trunk fails at or below certain critical temperature levels (from 25 to 30 C. in warm blooded animals). Refrigeration of an extremity abolishes pain and decreases the blood and lymph flow. Inhibition of the healing of wounds during refrigeration has been shown to occur.

The effect of the tourniquet on the progress of infection varies with the duration of the period of ischemia. If a tourniquet is applied tightly enough to a limb proximal to a gangrenous or affected area the obliteration of vascular and lymphatic channels at the level of constriction will prevent the absorption of toxins and bacteria from the involved region into the general circulation. This beneficial effect will continue as long as the tourniquet is in place.

The survival of a tightly constricted limb is prolonged greatly by refrigeration of the part. The benefit of refrigeration with the application of a tourniquet below the proposed level of amputation

of a limb has included loss of sensation and elimination of absorption of noxious agents from the part the further advantage of elimination of interference with wound healing and of spread of infection is also assured.

The management of critically ill patients with gangrenous extremities frequently involves the control of toxemia of infection of anemia, and of derangements in metabolism. Six cases are presented in which gangrene of one or both feet was associated with infection and toxemia. The patients were operated on without mortality and without interference with subsequent wound healing. It was believed justifiable, therefore, to advocate the use of the method. The detail of the technique used was described. Refrigeration was not used in any case unless the patient's condition was so poor due to severe infection and absorption from the gangrenous part, that the ordinary methods of treatment seemed dangerous.

MARY KARP M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Kulowski, J. French, A. M., and Erickson, H. R.: *Aire Lite. A New Plastic Medium of Clinical Immobilization.* *Am J Surg* 944 66 315

Methods of immobilization form an interesting chapter in the history of clinical surgery. Modern methods received their impetus in 1834 when Sue tin's "starched apparatus" first appeared. Plaster of Paris bandage was invented by Matthysen in 1852. The excellent results obtained with the latter medium induced surgeons to overlook some of its disadvantages. The main disadvantages are its relatively heavy weight and bulk, its poor penetrability to the x rays, the general untidiness attending its application, wearing and removal, the occasional trickiness of its setting characteristics due to the qualitative differences that exist between the various grades of plaster, the poor ventilation and its poor resistance to moisture with a tendency to absorb moisture of all kinds, which results in irritation of the skin, discomfort to the patient, and softening of the plaster cast itself. Recent improvements in the plaster-of-Paris bandages and splints and in the plaster technique have overcome some of these disadvantages. Substitutes for plaster have been introduced, however, none has been widely accepted.

The present article contains an interesting discussion regarding Aire Lite. The principle of this type of immobilization was introduced some years ago when Roger Anderson made use of a plastic fabrication in the form of a dry open-meshed, flexible bandage, which could be applied to the body and then sprayed with a volatile setting liquid to form a rigid supporting structure. He succeeded in applying this principle for clinical purposes. Aire Lite is a stockinette form of bandage made by loosely knitting a yarn composed of a mixture of cellulose acetate and a regenerated cellulose rayon. This knitted bandage is processed to control shrinkage, setting, and drying characteristics. When in place, the band-

age is sprayed with a solvent mixture composed of a combination of volatile liquids with acetone as one of the active ingredients which initiates setting and drying until it becomes rigid.

The bandage is then unchanged in its chemical composition but its physical characteristics have been altered radically. The loosely knitted loops of yarn which previously gave great flexibility to the bandage now function as rigid strut members and make a strong open meshed supporting medium. This medium is mechanically efficient, very light in weight, resistant to moisture, nonresistant to x rays, and comfortable to the patient.

The present report is based on a series of 136 patients upon whom 200 plastic casts and miscellaneous apparatus made of Aire-Lite were employed. The authors have classified the cases for which Aire Lite was used: there were 86 fractures among which simple and compound injuries were evenly divided. In 22 cases Aire Lite was used as primary fixation at, and subsequent to, onset of treatment. Seventeen simple fractures and 1 compound fracture thus treated were acute. 4 of these needed manipulative reduction and fixation under anesthesia. The bones injured involved the hand in 5 instances, the ankle in 3, the lower radius in 3, and the sternum, the clavicle, shaft of the tibia and fibula, the head of the radius, the carpal scaphoid, and the body of the scapula in 1 case each.

In 64 fractures Aire-Lite was used subsequent to plaster or other methods of fixation which had been previously instituted as an alternative (secondary fixation) apparatus. Of these, 22 were simple fractures which had been present from several days, with little or no callus formation to variable stages of convalescence when Aire Lite fixation was employed. These comprised 10 simple fractures of small and irregular bones of the extremities and vertebral bodies, 4 of the lower radius, and 8 of the long bones. Forty-two compound fractures were secondarily immobilized by Aire Lite, 36 of these were severe. The vast majority involved the long bones and showed variable degrees of bony dissolution and osteomyelitis, with little or no evidence of wound healing or bony regeneration at the time fixation was begun.

Fifty miscellaneous orthopedic conditions included diseased static or mechanical conditions, and congenital anomalies and post-traumatic conditions of the locomotor system other than fractures for which immobilization was desirable.

The pathological lesions included hematogenous pyogenic osteomyelitis, tuberculosis, arthritis, and osteochondritis.

Among the static or mechanical conditions, lumbosacral low back pain and internal derangement of the knee joint were prominent.

The residual deformities included in this group were neurogenic, arthrogenic, and myostic in origin. One instance of bilateral congenital clubfoot was treated. In contrast to the group of fracture cases, the most of these miscellaneous cases were primarily fixed with Aire Lite.

Aire Lite cannot be expected to replace plaster. The use of Aire Lite fixation in acute fractures is not wholly practicable because of the time element involved; therefore, its use remains optional with the surgeon. Aire Lite can be used effectively as a cast, splint or other form of apparatus in a wide variety of orthopedic conditions. Instead of the primary use of plaster. The same alternative use of Aire Lite fixation in the convalescent stages of both simple and compound fractures has also been established.

Since Aire Lite is a synthetic plastic product of various inherent characteristics its use demands a definite technique. Atmospheric conditions may influence its behavior in practice and interfere with uniformity of its setting and drying. There is a reactive time lag between the bandage and the solvent as a cementing agent. Another problem is the variable tendency it has toward shrinkage and creepage which must be anticipated and guarded against by strictly observing a proper technique and keeping the patient under observation especially for the first twenty-four hours after a cast has been applied.

A study of the characteristics of Aire Lite brings out the following points:

1. An unhurried attitude and technique with calm and deliberate work is essential, and by all means gentle handling of the bandage.

2. There should be no stretching or pulling of the bandage into place because such tension results in

undue subsequent shrinkage when setting and drying have occurred. In order to go around prominent curves the bandage must be pleated, folded or cut partially or completely at that point and another section properly overlapped and directed must be begun.

3. There should be no molding or handling of the wetted bandage as prescribed for plaster since subsequent gelatinization and loss of porosity would result after the bandage had hardened. This technique requires smooth gentle pressure and stroking efforts toward adherence, with care to secure overlapping edges which require additional cementing fluid.

Aire Lite has some disadvantages but also great advantages. From the surgeon's standpoint the greatest drawback to Aire Lite is the longer period of time it takes to set and become rigid. To remedy this disadvantage improved methods of fabrication and technique are needed. Among the advantages of Aire Lite may be mentioned the following: the light weight, ventilation, resistance to moisture, nonresistance to x rays, general neatness attending its use and its acceptability to the patient—these are distinct advantages over plaster. At this particular time the advantages of Aire Lite accruing from its inherent resistance to moisture are noted under naval and similar sea going conditions. From the angle of air transport the light weight of Aire-Lite is no less important.

MATTHIAS J. SEIFERT, M.D.

PHYSICO-CHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Kautz, F. G., and Schwartz, L.: Intraocular Calcium Shadows; Choroid Ossification. *Radial* 27 944, 43 486

The authors give a rather comprehensive review of the literature dealing with the roentgen demonstration of calcium shadows in the eyeball. It appears from this review that although intraocular calcifications are often suspected on clinical examination and proved by subsequent dissection of the enucleated eye, their roentgen visualization is rare.

Twining and Shanks distinguish four groups of intraocular calcium shadows: (1) calcification of the lens, (2) ossification of the vitreous, (3) calcified atheroma of the carotid and ophthalmic arteries and (4) a shrunken calcified globe. According to Duke-Elder bony cataract is fairly common in the late stages of a complicated cataract. It is also a well established fact that the internal aspect of the choroid often forms the site of bone metaplasia. Samuels goes so far as to describe three types of choroid ossification: (1) plates of solid bone (2) thick shells and (3) spicules of bone.

The presence of choroid ossification is usually suggested by the history and physical examination. Blindness, cataract, and the demonstration of a hard intraocular mass in an atrophic bulb are signs strongly in favor of ossification as contrasted to glaucoma, sympathetic panophthalmitis, or tumor. Roentgen study helps to establish the diagnosis beyond doubt.

The authors found on the basis of their own material as well as that collected from the literature, that the roentgen findings of choroid calcification are rather typical. Usually there is a shrunken eyeball, a large central area of which is occupied by a well delineated fairly regular ovoid, circular or semi-circular dense (although not strictly homogeneous) calcium shadow. Sometimes the shadow assumes the shape of a ring a few millimeters thick. In a few instances metallic foreign bodies have been observed near the calcium deposits.

Anatomically these shadows correspond to the bell-like ossification of the choroid and of the lens. The smaller densities are the result of the extent of the choroid throughout the eyeball and occasionally of the invasion of the cornea.

The differential diagnosis of choroid ossification includes opaque and semiopaque foreign bodies, vascular calcifications phleboliths, orbital angioma, osteoma, and superimposed endocranial calcifications. Pfeiffer has also observed calcium deposits in congenital retinoblastoma in children.

From the technical standpoint the authors recommend that three methods be used for the roentgen visualization of intraocular calcifications: (1) the posteroanterior projection of the orbit, which offers the clearest view (2) the lateral projection as it is used

for the routine localization of foreign bodies and (3) the "bone free" projection, which permits a view of only the anterior two-thirds of the eyeball. The use of planigraphy and orbitography with air may still improve the roentgen demonstration.

Seven cases are reported by the authors in brief résumés and illustrated with typical roentgenograms. Several other cases have been seen in the past ten years but they have not been recorded. In most instances there was a history of foreign-body injury to the eye with subsequent infection and gradual loss of sight. Pain occurred only in the acute and subacute stages of infection. The patients eventually became accustomed to their condition and in only a few instances was enucleation of the eye performed.

A bibliography of 31 articles is appended.

T. LARCOMA, M.D.

Reinberg, S. A.: X-ray Diagnosis in Gunshot Wounds of the Abdominal Cavity and Its Significance in Field Surgery. *Brit. J. Radiol.* 1944 7 291

The author reports that on the battlefield, casualties with wounds of the abdominal cavity are transported to the x-ray department direct from the field, usually in the first twenty-four hours and often within a few hours of the injury. The vast majority arrive in comfortable transport, sometimes by plane.

They are examined in two positions: are not removed from the stretcher and are never made to stand. During the acute stage of their condition, no contrast substance is given internally, but shock is no contraindication to roentgenographic investigation. No x-ray examination of the abdominal cavity is considered complete unless the chest and pelvis are also examined, and if circumstances demand it, also the neck and shoulder girdle. Conversely with a wound of the chest and pelvis even when there are no special clinical indications the abdominal cavity is examined.

In the author's series of cases the vast majority of the patients had penetrating wounds. Perforating wounds were fewer and tangential wounds were rare. Shrapnel wounds were three and one-half times as frequent as bullet wounds, and fragments of artillery shells were found four times more commonly than fragments of grenades or mines. Of the bullets, the great majority were sharp-pointed and came from rifles and machine guns. The author had only 2 examples of revolver bullet wounds. Blunt-nosed bullets discharged by automatic hand weapons were frequently encountered. So far the author has seen none of the spherical shrapnel bullets that played such an important part in the last war.

In half of the cases of penetrating abdominal wounds the entry was in the lower part of the chest, usually at the level of the eighth to tenth ribs,

although sometimes higher. The entry wound was found in the anterior abdominal wall in one fifth of the cases. It is important to note that in two-fifths of all the cases the entry wound for a bullet penetrated the abdominal cavity was in the region of the pelvis.

It is difficult to decide the nature of the missile until a ray examination has been made. This is all the more important since shrapnel wounds have a much more difficult clinical course and a worse prognosis than bullet wounds. Shrapnel has a much greater tendency to pull fragments of soiled clothing into the tissues and thereby expose the patient to the risk of infection.

It is most difficult to locate foreign bodies in the abdominal cavity. The consequences of a penetrating wound are more important than its nature or its location. Roentgenological examination is undertaken primarily with the view of ascertaining the state of the abdominal cavity and its contents. The most important abdominal injury is a penetrating wound with perforation of the gastrointestinal tract. Interest centers chiefly on those clinical diagnostic signs associated with the escape of gas or fluid from the viscera into the abdominal cavity. Although the roentgenographic recognition of large amounts of gas is a relatively simple matter the demonstration of minute amounts requires exceptional technical skill and knowledge. Large amounts of gas can be demonstrated with the patient placed in any position but when small amounts are suspected the lateral view is indicated. This can be obtained with the patient on his back or on his side. With the patient on his back, quite small quantities of gas can be detected immediately above the liver dullness the so-called antehepatic pneumoperitoneum. This is the most natural position for the majority of cases but undoubtedly the most satisfactory and most desirable view is that taken with the patient lying on the left side. In this position the most minute amount of gas can be detected. This is the so-called extrahepatic pneumoperitoneum. In the majority of cases the patient was immediately subjected to a laparotomy in the course of which the diagnosis was invariably confirmed. In many cases there were so few clinical signs pointing to the presence of intestinal damage that no surgeon would have considered an operation if the presence of gas had not been demonstrated. The pneumoperitoneum is sometimes even more reliable than the visual examination at the time of operation. Of equal importance were the cases in which roentgenological examination proved to be negative in respect to pneumoperitoneum. Many cases were clinically so complex and difficult that only the radiologist's negative report prevented an operation and subsequent uneventful recovery confirmed these findings. There were occasions when a negative roentgenographic diagnosis of pneumoperitoneum was not confirmed by subsequent events. It must be noted that only about 55

per cent of cases of perforated gastric and duodenal ulcers produce a pneumoperitoneum.

The roentgenological investigation of liquid in the abdominal cavity is much more difficult than the demonstration of gas. The nature of liquid in the abdominal cavity cannot be determined roentgenologically, but it is clear that fluid found roentgenographically during the first few hours after an abdominal wound obviously is likely to be blood and thus this is an important sign of a penetrating wound. The nature of damage to solid internal organs cannot as yet be determined. Only superficial and border defects of the liver tissue can be detected. In the case of hemorrhage into the liver it is possible to demonstrate a total enlargement of the whole organ.

Because of the invariable practice of roentgenographic examination of the chest in cases of abdominal trauma, unsuspected conditions are sometimes brought to light and many of these are not demonstrated clinically.

As far as it is possible full roentgenographic facilities must be brought as near as practicable to the locality where abdominal injuries are likely to be found. It is essential that the interval between the time of injury and the institution of proper treatment should be reduced to a minimum.

HAROLD C. OCHSNER, M.D.

Peters, M. V.: Radiation Therapy of Carcinoma of the Breast. *Canad. M. Assn. J.* 1944, 51: 335.

In this article the author reports his results in radiation therapy of breast lesions during a two-year period evaluating the effect of 400 kv. on the various stages of malignant mammary lesions.

The statistical data show the relationship between age and survival, between rate of growth and survival and between the duration of the disease and survival. In addition the table which accompanies the article shows the most frequent sites of metastases.

The lesions of the breast were divided into three stages.

Stage I lesions consisted of those which were entirely within the mammary gland without fixation or evidence of extension. In this group the five year survival rate was raised from the average of 65 to 75 per cent chiefly by the use of postoperative irradiation.

Stage II malignancies included the lesions which were surgically difficult to remove and those in which a high degree of malignancy had been determined by the use of Lee and Stubenbird's table of clinical index of malignancy. In this group the five year survival rate was raised from 15 to 30 per cent.

Stage III carcinomas were the ones which were beyond help and in which radiation therapy could offer only palliative aid.

The author believes that preoperative irradiation particularly in stage II lesions would materially influence the end results. R. A. BRADY, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Davidson, L. S. P: *Nutrition and Diet in War Time*.
Edinburgh M J 1944, 51: 430.

A considerable section of the population of Britain was living before the present war on a diet which was inadequate to meet the optimal demands for growth and the maintenance of health. It is also clear that the dietary deficiency was mainly qualitative rather than quantitative. In other words, the caloric value of the diet was seldom at fault, the deficiency was essentially of vitamins, minerals, and to a less extent, of first-class proteins.

In arriving at any conclusion regarding the effect of war on the diet of the nation as a whole, two questions will have to be answered:

1. Have the restrictions imposed by war produced an undesirable reduction in the quality or quantity of the diet consumed by people whose intake of food was formerly unrestricted by economic circumstances?

2. Have the wartime food measures produced an improvement or a further deterioration in the diet of that section of the population which even before the war was unable to buy sufficient of the right kind of food to supply its nutritive requirements?

The second question is the more important, as the individuals in this section of the population had no nutritive "slack" to take up and any further deterioration in their diet would necessarily have led to such a serious increase in ill health that the morale and efficiency of the home front would have been undermined.

Since two-thirds of Britain's food was imported it was obvious that a serious reduction in the food supply would result as soon as the stocks of imported foods were used up unless drastic measures were instituted both to augment the supply of ships and to increase the production of certain foods, the balance being imported according to a plan designed on a scientific basis. The country was faced not only with a deficiency of such basic products as meat, fats, and cereals, but also of important protective foods such as the dairy products, fruit, and vegetables. The British Government decided that it was essential, in the first place to secure the caloric value of the nation's diet, and accordingly took steps to increase greatly the home production of food and to import the remaining requirements according to a scientific plan. An agricultural policy, which primarily concentrated on the production of cereals and potatoes was adopted. By 1943 the production of wheat, barley and oats in tons had been increased by 80 per cent and of potatoes 95 per cent. Since milk cannot be satisfactorily replaced by any food and cannot be imported from a distance in a fresh state, the maintenance of or

even an increase in, milk production was accepted as another essential feature of the wartime agricultural policy. This could be accomplished only by carefully controlling the plowing-up policy on dairy farms and by giving dairy cattle the highest priority in the issue of concentrated feeding stuffs. The production of milk has been maintained at the pre-war level, despite the great reduction of grass land. The consumption of liquid milk is actually 34 per cent higher in 1944 than in 1938, because the diversion of liquid milk to manufacturing purposes has been prohibited. The third essential feature of the food policy was an increased home production of green and yellow vegetables. By 1943 an increase of 33 per cent over the prewar consumption had been secured by a combination of methods including stabilization of prices, subsidies for the professional grower and propaganda directed toward the private individual with a garden or allotment.

The first priority on shipping had obviously to be reserved for wheat which is easily transported and stored and which constitutes the most suitable food for maintaining the caloric needs of the nation. The Government's decision to keep flour bread, and potatoes unrationed as long as was humanly possible was undoubtedly sound both on administrative grounds and because it ensured that no one needed to go hungry for want of energy-giving foods. The second priority was fats which have more than twice the energy value of carbohydrates, are valuable sources of fat-soluble vitamins, and take up relatively small amounts of cargo space. The third priority for importation was cheese, which is a particularly condensed form of food valuable for its fat, calcium, and protein content. The latter aspect was of especial importance because of the decision to reduce greatly the importation of meat. Meat is a foodstuff which is bulky and which requires special refrigeration facilities. The importation of fruit had to be almost completely abandoned because of its bulk and poor keeping qualities. With the object of increasing the carrying capacity of the ships available for the transport of food the bulk of the foodstuffs was, whenever possible, reduced by the processes of compression and dehydration (e. g. milk, eggs, fruit juice, and, recently meat) and by deboning the carcasses of animals. By increasing the extraction rate of flour from 70 per cent (white flour) to 85 per cent (National wheat meal flour) a greater yield of flour is obtained from a given weight of grain. The introduction of the 85 per cent extraction flour in 1943 not only saved several hundred thousand tons of shipping space annually but secured the vitamin B requirements of the nation and greatly augmented its supplies of iron and valuable vegetable protein.

Although the wartime diet is monotonous, it is adequate in so far as calories and protein are con-

ceded and it is superior to the prewar diets in respect to the minerals, calcium and iron and the vitamins of the B complex. Only in respect to vitamins A and C is there any reason to suspect its adequacy.

If the outbreak of the war it was apparent that particular attention should be given to certain classes of individuals whose demands for certain factors were enhanced because of their requirements for growth, pregnancy or illness. The nutritional factors of particular importance for these categories are first-class protein, calcium and vitamins A and C, a deficiency of which constituted a potential danger in the wartime diets. To prevent the development or minimize the effects of such deficiencies, the Government not merely undertook a campaign of increased production, as outlined but introduced special measures which gave a priority supply of food and vitamin supplements to these persons whose needs were greatest:

1. Vitamin A (as cod liver oil or halibut liver capsules), vitamin C (as orange juice, rose-hip syrup and black currant juice), and milk to pregnant and nursing mothers, infants and children under 5.

2. An extra half meat ration to expectant and nursing mothers.

3. Milk and meals in school for children of school age.

4. The setting up of industrial canteens and British restaurants where workers can obtain meals cheaply and in addition to the ration.

5. The provision of extra cheese rations to agricultural workers and miners who are unable to obtain meals at canteens.

6. Extra rations and special priorities to invalids and persons on special diets, e.g.

(a) Double meat and fat ration and extra cheese and milk ration to diabetics.

(b) Special milk allowance to patients with gastric diseases and patients suffering from tuberculosis.

(c) Extra meat rations to patients suffering from steatorrhea and hepatitis.

(d) Special priorities of milk, eggs and fish to hospitals, etc.

7. Compulsory fortification of foodstuffs, viz.

(a) Addition of vitamins A and D to margarine.

(b) Introduction of calcium into National Flour.

The effect of five years of wartime diet on the national health showed no decrease in the general economic efficiency. Despite the housing, transport and black-out difficulties, the productivity per head of population in Great Britain is stated to be the highest in the world.

The consensus of opinion among school teachers, social workers, school medical officers, and research workers who have carried out nutritional surveys is that the health of the children of Britain in 1944 is satisfactory. The Parliamentary Secretary to

the Ministry of Food stated in August, 1944 that a recent investigation of some 30,000 adolescent and adult males revealed no evidence of any loss of weight or unsatisfactory growth.

Despite the dangers of overcrowding and reduced ventilation due to the black-out, and shelter life the incidence of the majority of the common infectious diseases, with the exception of venereal diseases and tuberculosis, is actually less in 1944 than before the war.

The birth rate has increased and the death rate for the country as a whole has decreased.

Research workers, social workers and experienced clinicians alike are all agreed that frank deficiency diseases such as scurvy, beriberi and pellagra are as rare today in Great Britain after five years of war as they were in prewar days. Large-scale surveys of the incidence of anemia, as carried out by the writer as well as by others in Great Britain show that by and large the position in regard to iron deficiency anemia is satisfactory.

Flourid rickets is as rare today as it was in the immediate prewar period.

A survey carried out by M. Mellanby and H. Connolly on London County Council school children in 1943 under conditions of control and clinical assessment similar to those used in the same area in 1929 showed the percentage of teeth with perfect or nearly perfect structure was more than twice as great in 1943 as in 1929 while the percentage of very defectively formed teeth was reduced by approximately half.

The more fortunate members of society whose diet was formerly unrestricted by economic circumstances have had a reduction in their intake of many of the essential nutrients as a result of the war but the evidence adduced regarding national health shows that these reductions have done no material harm. In the small proportion of people who consistently ate and drank too much there has probably been an actual improvement in health. Improved economic circumstances, the more even distribution of essential foodstuffs brought about by rationing, the introduction of National Flour and the fortification of certain foodstuffs have certainly prevented any further deterioration in the diet of the less fortunate section of the population who could not buy an adequate diet before the war and in at least certain categories (pregnant women, infants and school children) have led to improvement.

War inevitably brings a great impetus to scientific research of all kinds. The success of the Government's wartime food policy can be attributed largely to the sound scientific basis on which it was founded. It is to be hoped sincerely that those wartime measures which have been shown to be of such value to the people's health, e.g. priority rations of milk for infants, school children and pregnant women, school meals and works canteens, and National wheatmeal bread will be continued as part of the permanent peacetime food policy.

CHARLES BARON, M.D.

Pijon, M., and Lozner E. L.: Vitamin C Economy in the Human Subject *Bull. Johns H. phys. Hosp.* 1944, 75, 303.

One subject was placed on a diet without vitamin C until there was a steady linear decline of the white-cell-platelet values of the blood. After twenty-one months on constantly maintained low values, no scorbutic manifestations had appeared and healing of an experimental wound appeared normal. Six subjects saturated with ascorbic acid for from four to six days were then placed on a diet which was normal as to a lack of vitamin C. None of the subjects developed scurvy until after five or six months had elapsed and they seemed normal in all respects until two weeks prior to the onset of the disease.

It seems that the adequate intake of vitamin C should be between the protective minimum (from 18 to 25 mgm. daily) and the amount required to maintain saturation as represented by excretion in the urine (from 80 to 100 mgm. daily). In the absence of clinical evidence the precise intake between the minimal protective dose and the saturation dose is largely a matter of conjecture. If a subject has been initially saturated with ascorbic acid and is then deprived of vitamin C, a period of protection against scurvy exists for as long as five or six months.

WALTER H. NADLER, M.D.

Nielsen, J. M.: A Subacute Generalized Neuromuscular Exhaustion Syndrome *J. Am. M. Ass.* 1944, 136, 501.

Four cases are reported of neuromuscular exhaustion followed by atrophy and fascicular twitching requiring months for recovery. This syndrome believed to be due to neuromuscular exhaustion has not been described in the literature.

Since the cases reported were not studied during the first weeks of the disability, no chemical studies were carried out. During a period of euphoria with oblivion to fatigue the individuals continued to work until the sudden onset of complete neuromuscular exhaustion approaching paralysis. Psychomotor restlessness continued, pains and tenderness were prominent, the muscles became flabby then twitched and atrophied. Paralysis supervened with great loss of body weight. Recovery was delayed for months. In the most severe cases the condition was not entirely overcome. Exacerbations were apt to follow relatively slight exertion. The patients were not neurasthenic and were inclined to ignore their disability.

WALTER H. NADLER, M.D.

Vieta, H. R.: Myasthenia Gravis Treated with Large Doses of Neostigmine Methylsulfate, Intramuscularly and Intravenously, and with Neostigmine Bromide Orally *Am. J. M. Sc.*, 1944, 208, 701.

An American of sixty-eight years, who had previously been a missionary in India with malaria and diarrhoea, presented a severe advanced condition of typical myasthenia gravis, for which he was given eight weeks of intensive treatment. At first he was

given neostigmine methylsulfate parenterally as he was unable to swallow medications but later he received neostigmine bromide orally. The results were reported in support of the author's contention as to the innocuity and nondevelopment of tolerance following heavy and long-continued dosage with this drug.

Three charts portray in detail the hourly (exclusively parenteral) administration of as high as 510 mgm. per twenty-four hours, of neostigmine methylsulfate for the first three weeks, with later total oral dosages of as much as 510 mgm. of neostigmine bromide as the patient improved. Finally the intramuscular injections consisted of 1 or 1.5 mgm. of the methylsulfate preparation and the intravenous administrations (of which there were not more than one per day) consisted of 1.5 mgm. of the methylsulfate in 1,500 cc. of 5 per cent glucose solution (in subsequent patients as much as 3 mgm.) reinforced with 100 mgm. of vitamin C, 10 mgm. of thiamine chloride, 100 mgm. of nicotinamide, and 10 mgm. of riboflavin, the rate of inflow being 70 drops per minute.

Acquired tolerance did not develop and intestinal stimulation was minimal; there were a few cramps, but only 3 to 4 soft bowel movements each day, without diarrhea. Atropine sulfate (1.6 mgm.) was given only 5 times in the eight weeks, on the other days a few drops of tincture of belladonna were substituted. At the end of eight weeks the patient was being maintained on oral neostigmine bromide as had been done for three months before he entered the hospital. He was now able to take as much as 2,400 calories of food daily and was nearly symptom free.

JOHN W. BRIDGMAN, M.D.

Winsor, T., and Dureh, G. E.: Differential Roles of Layers of Human Epigastric Skin on the Diffusion Rate of Water *Arch. Int. M.* 1944, 74, 424.

The diffusion and retention of water by the skin has been a generally recognized function which has not been investigated previously with the detail of the present report.

Diffusion water is defined as water that has passed through the skin to the atmosphere. It is differentiated from the water secreted by the sweat glands. The rate of diffusion of water was determined by means of a specially constructed collecting chamber sealed over the surface of the skin and fitted with an inlet and an outlet tube. The studies were conducted in a controlled air-conditioned room. The average rate of diffusion of water in 13 human subjects was 4.8 mgm. per 5 sq. cm. of surface area in ten minutes. This diffusion water originated from the blood of the skin. The average rate of diffusion of water for cadaver skin was 5.4 mgm. per 5 sq. cm. in ten minutes. With living skin when the temperature is raised past a certain point, secretion water from the sweat glands is also added. In a comfortable environment, the rate of diffusion of water through the skin of patients with atrophic sweat glands was of the same level as that through normal skin. The rate of diffu-

skin through the skin freed from the underlying tissue of fascia, muscle or peritoneum was the same as for skin with its underlying tissues attached. With the epidermis removed the average rate of diffusion was approximately 10 times that of normal skin and indicated that the diffusion restraining layer was located within the epidermis.

After blister formation the rate of diffusion through the denuded surface averaged 41 ± 2 mgm. for 54 sq. cm. in ten minutes. In the latter experiments it was also indicated that the portion of the epidermis superficial to the stratum spinosum contained the inhibiting layer. Tissues or organs without epidermal structures such as the ventricle, the spleen and the placenta, showed no inhibition to the diffusion of fluid. The rate of diffusion of water through the superficial layers of the epidermis contained in the roof of the blister averaged 4.5 mgm. per 54 sq. cm. in ten minutes, almost the same as that through normal intact skin. This finally localized the water withholding function to the keratinized epithelial cells. The inhibiting influence from the colloids of the blister fluid were ruled out. Removal of the corneal layer of the skin by sandpapering resulted in a marked increase in the rate of diffusion of water similar to that obtained after removal of the epidermis by chemical blistering. By other exclusion experiments such as rubbing the skin with gauze it was proved that erythema in itself did not increase the rate of diffusion. Removal of the superficial lipids of the skin with acetone and ether showed that diffusion through defatted skin was essentially similar to that from normal skin. In summary the keratinized portion of the epidermis conserved water loss by inhibition of the diffusion of water. These experiments should be of value in the study of burns.

B. G. P. SHAPIROFF M.D.

Burch, G. E. and Winsor T. The Rate of Insensible Perspiration (Diffusion of Water) Locally Through Living and Through Dead Human Skin. *Arch. Int. M.* 1944, 74: 437

Perspiration has been defined as either insensible or sensible. Included in the term of insensible perspiration is diffusion water which must be differentiated from the secretions of the sweat glands. The rate of diffusion of water is influenced by air currents, temperature of the skin, relative humidity, and the electrolyte and protein concentration of tissue fluids. The rate of loss of water through dead skin at the temperature of the normal environment was found to be 5.4 mgm. per 54 sq. cm. per 10 minutes. The accumulation of sweat on the surface of the skin of resting subjects in an environment of 35°C. and 50 per cent relative humidity constantly averaged about 1.5 mgm. When this saturation level was reached it remained constant thereafter. The mean rate of flow was approximately the same in the negro as in the white man which excluded pigment as a factor. The rate of loss of water was not affected by the period of storage of the skin in the refrigerator and the subsequent thawing. In the

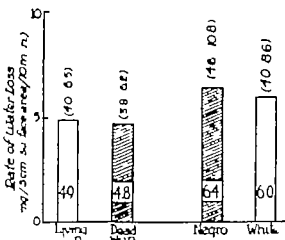


Fig. 1. The rate of loss of water through skin of the epigastrum of living subjects resting quietly in bed in a comfortable environment through dead skin of the epigastrum through dead skin of the negro and through dead skin of white subjects. In this figure the mean values are indicated in the center of each column and the extreme values at the top.

latter experiments, the water of diffusion through dead skin excluded any secretion by the sweat glands. It was also found that as the temperature of the dead skin was raised the rate of diffusion of water increased. In a simultaneous study of the loss of water through living intact skin and dead isolated skin there was no significant difference between the two. Other experiments also proved that the water collected from the skin of a subject resting quietly in a comfortable environment was purely that of water of diffusion. The rate of loss of water through the surface of the cover of a large blister showed no significant difference from the rate of loss from the intact normal skin. In 2 subjects with severe atrophy of the sweat glands the rate of water diffusion was the same as that obtained for dead skin in which the sweat glands do not function.

B. G. P. SHAPIROFF M.D.

Spiegel, E. A., Oppenheimer M. J., Henny G. C. and Wycis, H. T.: The Experimental Production of Motion Sickness. *War Med. Ch.* 1944, 6: 283

Motion sickness (kinetosis) embraces syndromes such as seasickness, airsickness, car sickness and railway sickness that are induced by similar mechanisms namely repeatedly accelerated and decelerated linear or rotatory motions; these motions are often but not necessarily oscillating.

The testing of a person's susceptibility to motion sickness or changes of this susceptibility under therapeutic measures can be done by means of the Bárány chair. However this chair fulfills the requirements only partially as an angular acceleration is produced only at the beginning and a deceleration at the stopping of the rotation and the spatial relationship of the various parts of the labyrinth to the axis of rotation remains constant during rotation.



Fig. 1. Rotating tilting apparatus for the production of motion sickness. A, Posterior view; B, base; C, side view.

For a quantitative test, changes in position of the head as regularly as possible and in definite directions are necessary. In order to obtain this feature the authors designed the chair and accessories as seen in the accompanying illustration. By the many electrically driven mechanisms, the head is tilted with each turn either in the sagittal or in the frontal plane, so that the angle between the plane of rotation and the plane of the horizontal semicircular canals regularly increases and decreases during each rotation. The same applies to the vertical canals. The effect on the respective canals is the same as if the speed of the motion were regularly changed. In those phases in which certain canals, e.g. the horizontal canals, are most nearly parallel to the horizontal plane the speed of the endolymph movement in these canals is increased; in those phases in which these canals approach the vertical plane, the endolymph movement in these canals is retarded. Thus at regular intervals, the effects of angular acceleration and deceleration on the endolymph flow are produced, and thus the labyrinths (the horizontal as well as the vertical canals) are subjected to mainly the same type of stimulation as in motion sickness.

The rhythmic tilting of the head furthermore produces rhythmic up and down movements of the labyrinths, a type of stimulus occurring not infrequently, e.g. in seasickness (up and down movements of the ship). Thus the labyrinth is subjected to a combination of stimuli.

Symptoms of motion sickness are produced within eight minutes. A comparison of the results with previous experiences of the subjects showed that the weaker method of stimulation (rotation combined with sagittal movements of the head or body) was sufficient to reveal a high degree of susceptibility. The stronger stimulation (rotation combined with frontal head movements preceding or succeeding rotation combined with sagittal head movements) was effective in nearly all moderately susceptible persons and produced symptoms even in some of the persons who were supposedly not susceptible according to previous experiences.

Optic fixation of an object that participates in all movements of the head tends to diminish the inci-

dence of motion sickness as compared with optic fixation of a stationary object situated somewhere in the surroundings.

Typical illusions of spatial orientation were produced. Their appearance was independent of that of the vegetative symptoms of motion sickness, which indicated that two somewhat independent mechanisms are involved.

Symptoms of motion sickness may be elicited not only by stimulation of the maculae but by stimulation of the cristae ampullares.

STEPHEN A. ZIEGLER M.D.

Cameron D. Rodent Ulcer Treated by the Application of Sodium Bicarbonate. *Lancet* Lond 1944 720.

After the local application of sodium bicarbonate in the treatment of rodent ulcer the lesion disappeared in 8 of 16 uncomplicated cases; this was verified histologically.

The sodium bicarbonate was applied on white lint as a simple saturated solution in water, as a water saturated solution with glycerin added to prevent drying, or as water-glycerin lotions or pastes of various strengths. It has also been used as an ointment with 15 or 30 per cent in lanolin, eucerin or soft paraffin. The solutions or pastes were found to be more effective than the ointments.

When solution alone was used there was little or no obvious reaction. When a strong paste was used, the area around the ulcer became red and purulent material came away from the base; this was followed by separation of a slough and exudation of serum. The application of the solution at this stage should result in healing.

Since the salt used is bland, the results obtained are not due to any caustic action. The fact that healing takes place shows that only the malignant tissue is adversely affected by the solution. The action of the sodium bicarbonate may be either direct or indirect. If the action is direct, it may be physical or chemical. Physically the sodium bicarbonate may increase the osmotic pressure of the lymph in which the cancer cells are bathed, and thus damage them. Chemically it may act by heightening the

alkalinity of the lymph. By altering the pH it may inhibit the action of some enzyme, such as the proteolytic one, which constitutes the diffusion factor. If the action is indirect, the salt may by virtue of its solvent properties, remove a local stimulating substance, which has set up carcinogenesis. With removal of the irritant the malignant bias might be gradually reversed.

Whatever the action of sodium bicarbonate it seems to be different from that of radium. It does not impair the effect of radium, and is not prejudiced by the previous use of radium.

The salt may fail in its effect because interposition of fibrous tissue or healthy epithelium prevents its access to the malignant cells or their immediate surroundings.

SAMUEL KAHN M D

Gore, I., and McCarthy A. M : Boeck's Sarcoid. *Surgery* 1944 16 865.

Boeck's sarcoid has come to be regarded as a relatively benign disease of obscure etiology having a predilection for lymphoid tissue but capable of involving any tissue in the body. Despite this potentiality a large proportion of the cases reported are characterized by skin lesions, regional or generalized lymph-node enlargement, a stringy or milky infiltration of the lungs, and cystic changes in the long bones of the hands and feet. In each of these structures the pathological identifying factor is the "hard tubercle" formed of a nodular aggregation of plump polygonal, acidophilic epithelioid cells identical with those found in tuberculosis.

Although lesions have been found in almost every tissue of the body clinical symptoms pointing to involvement of the intestinal tract have not previously been reported.

The authors treated a twenty-six year-old soldier with complaints of burning and sometimes gripping pains in the epigastrium after meals. The symptoms which started June, 1941 were associated with belching and the eructation of bits of food and bitter, hot, slimy material. The patient noticed a loss of weight from 186 pounds in May 1942 to 168 pounds on December 7, 1942. In September 1942 he began to vomit occasionally following meals. Postprandial vomiting became more frequent until the time of hospitalization in December when he could retain very little. The epigastric pain at this time was more or less continuous, both day and night.

Positive findings were limited to moderate emaciation, venereal warts of the prepuce, and moderately enlarged inguinal lymph nodes. Roentgenological examination of the gastrointestinal tract revealed a permanent cone-shaped deformity of the pyloric antrum through which only very shallow peristaltic waves traveled. This rigidity suggested an intramural infiltration of some kind, probably neoplastic in nature. There was no evidence of ulceration or of four hour gastric retention. Stools were negative for occult blood. Three successive positive Wassermann and Kahn serological reactions in January 1943 were reported and syphilis of the stomach was

considered even though the roentgenological findings were not suggestive of this disease. Gastric analyses showed an absence of free hydrochloric acid after histamine the total acidity reaching a maximum of only 20 units. Because the patient failed to respond to antisyphilitic therapy the impression at this time was that he had a gastric neoplasm.

Laparotomy revealed a diffuse doughy thickening of the pyloric stomach. Both the anterior and posterior walls were involved, as well as the greater curvature. The lymph nodes along the omental attachment were markedly enlarged the other viscera appeared normal. Biopsies of the thickened stomach wall and of an enlarged lymph node were taken for frozen section. These revealed the inflammatory nature of the lesion and a provisional diagnosis of gastric tuberculosis or sarcoid disease was made. A gastric resection was performed with the Balfour Polya type of anterior loop anastomosis. Postoperative convalescence was uncomplicated.

The histological diagnosis was (1) Boeck's sarcoid of the stomach and lymph node and (2) subacute ulceration of the pyloric stomach. The preoperative diagnoses considered were peptic ulcer gastric syphilis and gastric neoplasm. Ulceration was undeniably not demonstrated by means of x rays since the ulcer was shallow and its position on the greater curvature did not lend itself to easy demonstration. Furthermore, the presence of achlorhydria, the position of the lesion, and the lack of melena appeared to corroborate the negative roentgenological findings. Peptic ulceration was therefore considered unlikely.

Gastric syphilis was considered a likely possibility because of a rising serological titer, the relative youth of the patient and the position of the lesion in the distal portion of the stomach. However gastric syphilis is considered to be a manifestation of the tertiary phase of the disease. Nonetheless it was considered advisable to institute a therapeutic test of antisyphilitic treatment. There was no response to a short intensive course and after four weeks laparotomy was performed, the presumptive diagnosis being gastric neoplasm.

It is not possible to draw any conclusions as to treatment from one case of surgical sarcoid disease. Each case must be individualized. Although there is a strong tendency toward spontaneous resolution in the primary disease, it is the secondary complication which makes the case "surgical" that must be gauged in treating the patient.

JOSEPH K. NARAT M D

Stuart, B. M : The Sarcoidosis of Boeck. *Am. J. M. Sc.* 1944, 908 717

The condition diagnosed as sarcoidosis of Boeck in young negroes (3 males, 1 female) is reported not because anything could be added to what other writers have offered, but to record the odd coincidence in this small group (3 exemplars) of the urveoparotid syndrome of Heerfort. All 3 patients complained at the time of hospitalization of vague

tuberculous like symptoms such as loss of weight cough of a chronic character and enlarged lymph nodes. Leucopenia and eosinophilia were demonstrable in all, and in each case roentgenographic examination of the chest revealed bilateral hilar enlargement and infiltration in both lungs. In fact, in case 3 tuberculosis was demonstrated later. Biopsy of a lymph node in the girl and in 1 of the boys revealed an almost complete replacement of the normal lymph-node architecture by small and medium-sized circumscribed areas composed chiefly of large epithelioid cells arranged in a concentric manner with a moderate number of lymphocytes near the periphery. Fibers of hyaline connective tissue surrounded each lesion and delimited it from its neighboring lesion. Giant cells were present in an occasional lesion. Caseation necrosis was minimal and present only in a few of the circumscribed areas.

In 1 of the young men the eyes were apparently not involved, while in the young woman and the other male there was unmistakable evidence of the eye involvement characteristic of Heerfordt's syndrome. Slit lamp studies of the girl's eye on the right side revealed numerous grayish, keratic precipitates of various sizes, and inflammatory cells in the aqueous humor. In the boy both eyes were involved, while in the girl only the right eye showed involvement; however, in the latter even macroscopically there was observable a large inflammatory cauliflower cyst of the iris at 7 o'clock near the margin and a smaller cyst of the iris at 5 o'clock nearer the base.

In the girl both lacrimal and both parotid glands were enlarged but not tender. In 1 male the cervical, axillary, epitrochlear and inguinal lymph nodes were moderately enlarged, but neither the lacrimal nor parotid glands were involved. In the other male (the other case of Heerfordt's syndrome) there was a generalized enlargement of the cervical lymph nodes; however, there was only a suggestive enlargement of the right parotid gland.

JOHN W. BREDMAN, M.D.

DUCTLESS GLANDS

Lipton, R. W., and Abel, M. S.: Aspiration Biopsy of the Thyroid in the Evaluation of Thyroid Dysfunction. *Am J Med Sci.*, 1944, 208: 736.

Numerous clinical and laboratory tests for the diagnosis and evaluation of thyroid dysfunction are in use. There is a group of cases, however, in which the laboratory and clinical findings are at variance, hence a definite diagnosis cannot be made. The basal metabolism test, which is the standard procedure for laboratory diagnosis, has certain limitations in its interpretation. Two other valuable laboratory procedures are the determination of the blood-cholesterol levels and the galactose-tolerance test, but these like the basal-metabolism test, are affected by extra-thyroid pathology. Other laboratory and clinical tests have been found to be limited in their scope and interpretation.

The direct method of tissue examination is the final diagnostic criterion. Diagnosis by means of biopsy is the most accurate. When the tissue can be approached easily enough of an excision can be made for ordinary histological section. More inaccessible tissue can be obtained by aspirations with a needle and syringe. The principal difficulty with aspiration biopsies is the very small amount of tissue obtainable which often makes the ordinary histological diagnosis unsatisfactory.

Abel has introduced a method of histological diagnosis of thyroid disease which is based on a microscopic examination of the thyroid acinar cells. Since this method utilizes the dimensions of the cells themselves, and not the general architecture of the gland, it can be used with very small amounts of tissue, and suggests that aspiration biopsies can be used for the direct diagnosis of thyroid disease.

In order to make the aspiration biopsy for thyroid diagnosis as simple and as atraumatic as possible, the authors have developed the following technique:

A No. 18 or a No. 16 gauge 2 inch intravenous needle and an ordinary 30 cc. syringe are used. It is necessary for the needle to be sharp and the syringe to be fairly new so that the barrel and piston do not fit loosely. Tissues obtained are placed in 5 per cent formalin and are treated as regular paraffin sections to insure uniformity of results. A sedative may be given to the patient twenty minutes before the aspiration. The patient should be lying flat with the neck slightly hyperextended. The gland is palpated and a small area in the midline of the neck close to the gland is prepared aseptically and a wheal is raised in the skin with 1 per cent procaine. Some of the solution is injected continuously along the line of the intended puncture down to the gland. A small nick is made through the skin with a bistoury-pointed scalpel (No. 11 B P blade) with the instrument held at right angles to the skin surface. This puncture of the skin facilitates insertion of the needle and prevents its becoming plugged with surface epithelium. The needle with the syringe attached is introduced tilted at about 30 degrees to the sagittal plane. It is advanced slowly through the superficial tissues until the point is felt to enter one or the other of the lateral lobes, whichever seems the more accessible. This technique will avoid the trachea, and the other important structures as shown in Figure 1.

The extreme care with which this aspiration biopsy must be done is apparent from the amount of description of the procedure given by the authors.

Microscopic examination of the aspiration specimens shows only small particles of the gland in a large amount of blood. Closer examination under the oil-immersion lens reveals that these gland particles consist entirely of acinar cells, arranged in acini and portions of acini from which the colloid material is entirely gone. Apparently the force of the aspiration is chiefly exercised on the cells and the colloid is squeezed out and left behind. If only single cells are left, the acinar cells appear to be intact and undistorted in their acini and remnants of acini.

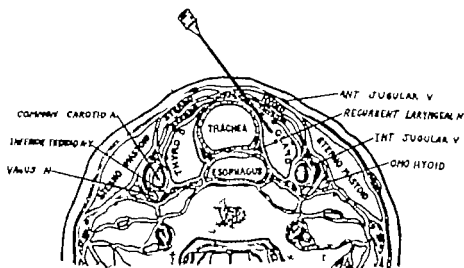


Fig. 1 Transverse section of neck at level of sixth cervical vertebra illustrating an aspiration needle in place

Abel used the criterion that an average cell height of over 5.8 units indicated toxicity in nodular goiters, a height of over 5 units indicated toxicity in diffuse goiters, and a height of less than 5 units indicated a normal gland. Each of his units equalled 1.4 microns which gives us the following standards to go by:

1. An average cell height of over 8.1 microns indicates toxicity in nodular goiters
2. An average cell height of over 7 microns indicates toxicity in diffuse goiters.
3. An average cell height under 7 microns indicates a normal gland. These standards for cell heights were used as a criterion for diagnosis. The measurement of the thyroid acinar cells as described by Abel was performed with a micrometer scale fitted into the eyepiece of the microscope, which was used on an oil immersed objective. In all cases the diameter of a cell was measured at a point crossing the nucleus and on a line along the radius of an acinus. The cells were measured in blocks of 100 from 100 separate acini chosen at random where the scale happened to fall as the slide was systematically moved across the stage. The only provisos were that the acini be open and that the cell boundaries be distinguishable.

By means of this procedure aspiration specimens from 20 thyroid glands were examined microscopically and 100 acinar cells measured from each. Later sections from surgical specimens were studied from each of 17 glands and in each instance 100 acinar cells were measured and the results compared with those from the aspirations and with clinical data. The measurements obtained from the aspiration specimens agreed very closely with those from the surgical specimens. It was found that a diagnosis of toxicity could be made on 16 of the first 17 aspiration specimens by the measurements alone. Aspirations done on 3 normal cases likewise confirmed the accuracy of the test and helped to confirm the standards for cell heights used as the criterion of

diagnosis. The average cell heights in these instances were all under 7 microns as would be expected in normal cases. In the cases described the measurement of acinar cell heights of thyroid aspiration specimens were of the magnitude expected and confirmed the diagnosis of toxicity in a majority of cases.

The present direct method may prove to be a valuable adjunct in the diagnosis of thyrotoxicosis

MATHIAS J. SEEVER, M.D.

Pomberton J. deJ. and Black, B. M. Goiter in *Children Surgery* 1944, 16: 756

From 1908 through 1943 189 children fourteen years of age or less with exophthalmic goiter were seen at the Mayo Clinic. In most cases thyroidectomy was carried out at the clinic, but 14 patients were treated medically with results that were considered good in 10 fair in 3 and poor in 1. Thyroidectomy was performed in 164 patients 8 dying while in the hospital. Fifty-five patients were operated on during the period before medication with iodine was instituted with 5 deaths. One hundred and nine children were operated on after having been prepared for operation with iodine with 3 deaths, a hospital mortality rate of 2.8 per cent. Since the preoperative use of iodine the late results after thyroidectomy have been satisfactory. Of the group of 102 patients who survived operation done since the use of iodine was instituted and on whom follow up data are available 1 died from the results of hyperthyroidism, 7 have had recurrent exophthalmic goiter and 23 have developed low basal metabolic rates or myxedema.

Fifty-two children, fourteen years of age or less with adenomatous goiter were seen at the clinic from 1917 through 1943. In no case was the basal metabolic rate elevated. Adenomatous goiter with hyperthyroidism has never been encountered in children at the clinic. Fourteen patients were operated on and the remainder were treated medically. The adenomas

seemed to differ in no way from those found in the goiters of adults.

From 1908 through 1943 a total of 53 children with nodular goiters were operated on. In 31 cases the nodularity was caused by adenomas in 3 cases by thyroiditis, and in 18 cases by malignancy. In 5 cases of carcinoma, enlarged cervical lymph nodes overshadowed the enlargement of the thyroid, but in the other 13 cases the nodularity was largely confined to the thyroid gland. Thus, 1 in 3 nodular goiters in the children operated upon were malignant.

In 17 of the 18 children with carcinoma of the thyroid gland, the tissue diagnosis was adenocarcinoma of either grade 1 or grade 2 malignancy. Thirteen of the adenocarcinomas were of the papillary type and 2 were noted to have developed in fetal adenomas. In 1 case the adenocarcinoma was of grade 4 malignancy. The lesion was judged operable in 10 cases and inoperable in 8. In every case in which metastasis had developed, 11 in all, the cervical lymph nodes were involved in 4 cases pulmonary metastasis developed and in 1 case metastatic tissue was found in the calvarium and in the spinal column. Whether or not the lesion was resected irradiation therapy was carried out in all but 1 case in which death occurred following biopsy.

Beardwood, J. T. Jr., and Levinson D. C.: Thiouracil in the Medical Management of Hyperthyroidism. *P. amsyloids M J* 944, 43 12.

The authors have used thiouracil in 30 cases of thyrotoxicosis, the duration of treatment varying from four to nine months. The series includes diffuse hyperplastic glands, toxic adenomas, and adenomatous colloid goiters. In 18 of the 30 patients the basal metabolic rate returned to normal, accompanied by clinical remission, weight gain, and elevation of the serum cholesterol. Therapy in 1 patient was discontinued because a leucopenia developed after the basal metabolic rate had fallen from plus 73 to plus 37. The time necessary for the basal metabolic rate to return to normal varied from one to fourteen weeks. Three patients requiring more than seven weeks for the return of a normal metabolism had been on iodine therapy prior to the thiouracil treatment. This confirms the findings of others that previous iodine therapy tends to delay the response to thiouracil.

In 4 of 5 patients whose treatment with thiouracil was stopped relapse followed but this was promptly controlled by the resumption of therapy. It appears advisable to give a maintenance dose of thiouracil over a long period, in an attempt to tide the patient over until the disease has exhausted itself rather than to employ intermittent therapy.

All patients were treated initially with gm. of thiouracil daily in 5 divided doses. The dosage was reduced as the basal metabolic rate dropped when this became normal a maintenance dose of from 0.1 to 0.4 gm. daily was given.

The only serious complication was leucopenia, which developed in 3 patients. Other transient reac-

tions which disappeared during continuance of the treatment were periorbital edema, leg edema, and hoarseness. A lower initial dosage should tend to diminish the frequency of these reactions. Metabolic studies of the serum cholesterol, urinary creatinine excretion and galactose thyroid function indicated the action of the drug to be physiological. There were 3 thyrocardiac patients in the series, all of whom were in decompensation. With thiouracil, the basal metabolic rate returned to normal, the heart action became less forceful, and the auricular fibrillation reverted to normal sinus rhythm. Thiouracil will probably find its greatest value in the management of thyrocardiac patients, who are frequently inoperable.

JOHN L. LINCOLN, M.D.

Rosa, E., and McConnell, J.: Thiouracil in the Treatment of Thyrotoxicosis. Clinical Experience with 37 Cases. *Am. J. M. Sc.*, 944, 308, 561.

In 1943 Mackenzie and Mackenzie, and Astwood and his associates first reported in detail the striking effects of thiourea and related compounds upon the structure and function of the thyroid gland in lower animals. Thiourea and its related compound, 2-thiouracil, inhibit the synthesis of the thyroid hormone, probably by affecting an enzyme system in the gland which normally aids in the conversion of iodine into the completed hormone.

The authors describe their clinical experiences with 37 thyrotoxic patients treated with 2-thiouracil. Thirty patients (81 per cent) showed a favorable response, 4 (10.9 per cent) showed a partial response, and 3 (5.4 per cent) showed no response to treatment. Three of the 6 patients showing unsatisfactory response presented associated conditions which may have influenced their reactions.

In 4 patients thiouracil was used during their preparation for thyroidectomy. One of these died twenty hours after operation, but the thiouracil was not regarded as a factor in the death. Autopsy in this case showed no lesions which could be associated with the use of thiouracil.

The control of thyrotoxicosis with thiouracil in a thirteen year-old girl with diabetes mellitus was not followed by an increase in carbohydrate tolerance or a decrease in insulin requirement.

The histological appearance of the thyroid gland in patients prepared for thyroidectomy with thiouracil showed the hyperplasia and other changes previously reported by others.

Eight patients have shown remission of their toxic symptoms for periods varying from three weeks to seven months following the complete withdrawal of thiouracil on minimal doses (from 0.1 to 0.5 gm. daily). 3 patients have responded likewise. Thirteen patients relapsed when the drug was either reduced in dosage or withdrawn. All of these patients, however, again responded to readministration of the thiouracil.

Measurements of the cardiac output by means of the ballistocardiogram in 9 patients showed a general

tendency toward a reduction in output under thionuracil therapy which was roughly parallel to the decline in the basal metabolism

No evidence of the development of refractoriness to thionuracil was observed. Untoward reactions attributable to the drug occurred in 8 patients. The most important of these was neutropenia with pharyngitis and fever noted in 2 cases. Reduction in the size of the thyroid gland was noted in 8 patients after prolonged treatment. Exophthalmos tended either to remain stationary or to increase slightly.

The authors raised a number of important questions regarding the effect and clinical usefulness of thionuracil. Among these are

1. What late toxic effects may follow its prolonged use? Is it possible for example that depression or exhaustion of the bone marrow might follow the prolonged ingestion of the drug in some cases?

2. What undesirable dislocations of endocrine relationship might be induced by prolonged inhibition of the thyroid-pituitary balance? Is there thus a possibility that hyperfunction of the pituitary might eventually be produced or that pituitary exhaustion might ensue? Is it possible that the maintenance of a chronically hyperplastic state of the thyroid might be followed by fibrosis atrophy or neoplastic change?

3. What is the effect of thionuracil upon the structure and function of the normal human thyroid gland? Much additional work appears desirable to explain the discrepancy between the consistent effects of thionuracil in normal lower animals and its apparent lack of effect of the normal human being.

4. What types of thyrotoxicosis will respond best to thionuracil, and how long must such cases remain under treatment before a permanent cure is effected?

5. Could the therapeutic response in thyrotoxicosis be enhanced by the coincidental use of anti-pituitary agents such as irradiation, estrogens or nadrogens?

The ability of most patients to remain ambulatory or even to continue at work, while under treatment for long periods of time constitutes an important advantage. Bed rest at the initiation of treatment shortened the time of response.

The authors come to the tentative conclusion that the drug effectively controls most of the phenomena of thyrotoxicosis in the large majority of patients and that its use at present is justified in the protracted treatment of mild or moderately severe cases and in the preoperative preparation of selected patients for thyroidectomy. It may also prove of considerable value in patients regarded as unacceptable surgical risks.

JOSEPH K. NARAT M.D.

Coburn, D. E.: Severe Osteitis Fibrosa Cystica with Parathyroid Tumor. Report of a Case of Fifteen Years Duration. *Am. J. Surg.*, 1944, 66: 352.

A severe case of generalized osteitis fibrosa cystica due to parathyroid adenoma is reported the tumor being located in the superior mediastinum. The case

was remarkable in that the symptoms dated back over a period of nearly sixteen years during which time the patient suffered 4 fractures and 1 operation for kidney stones. The skeletal involvement was extensive and included both patellae a site which has not been previously reported. Postoperative convalescence was marked by a fracture of the right femur which suggested that in the postoperative care of these patients precautionary splinting might be applied to the bones of the extremities which are extensively involved until some degree of recalcification has occurred.

SAMUEL KAHN M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Fleming, A.: Micromethods of Estimating Penicillin in Blood Serum and Other Body Fluids. *Lancet* Lond., 1944, 247: 630.

There is no chemical test for penicillin in blood, but the concentration of this substance in blood serum can readily be estimated by titration of its bacteriostatic power on a suitable test organism. This titration can be done in test tubes with volumes of 0.5 c.c.m. or 1 c.c.m. However since blood specimens have to be taken at frequent intervals and since large amounts of blood are required for the tests, this procedure was considered unjustifiable.

Microtitration tests have previously been described but they have now been modified. The detailed technique for performing microtitrations of penicillin in the body fluids of patients who are being treated by the drug is given. In this technique, slide cells or capillary tubes are used as cultural vessels the hemolytic streptococcus is the test organism and blood is the indicator.

SAMUEL KAHN M.D.

Troll, M. M.: Aberrant Pancreatic and Gastric Tissue in the Intestinal Tract. *Arch. Path. Chic.* 1944, 38: 375.

The presence of ectopic tissue in 8 cases is reported. In 3 cases the tissue was pancreatic, occurring in Meckel's diverticulum in 2 instances and in the ileum in 1 instance. In 6 of the cases gastric mucosa was observed in Meckel's diverticulum, and in 1 of these cases the diverticulum contained both pancreatic tissue and gastric mucosa. The 3 instances of aberrant pancreas in Meckel's diverticulum are the twenty fourth and twenty fifth cases to be reported while the case of pancreatic tissue in the ileum makes the twenty first in the literature.

The theory that the tissue was transplanted from the original site during embryonic development is believed to be the most acceptable of the 3 theories on the pathogenesis of the aberrant pancreas and gastric mucosa which were reviewed.

WALTER H. NADLER, M.D.

Schrek, R.: The Racial Distribution of Cancer II. Tumors of the Kidney Bladder and Male Genital Organs. *Ann. Surg.*, 1944, 120: 809.

The incidence of cancer of the genitourinary tract in the white and colored races was studied indirectly

by the method of determining the percentage of colored patients in the tumor and in the control groups.

According to this study cancer of the penis and scrotum, and possibly cancer of the prostate, occurred relatively more frequently in colored than in white men. Colored men below the age of fifty had a relatively low incidence of cancer of the testis but negroes above the age of fifty had the same incidence of this tumor as the white men. Colored men, but not colored women, had a relatively low incidence of cancer of the bladder. Tumors of the kidney occurred equally frequently in white and colored individuals.

JOHN J. MALOWY, M.D.

EXPERIMENTAL SURGERY

Large, A. and Heinbecker P: The Effect of Cooling on Wound Healing. *Ann. Surg.* 944, 120 7 7

Experiments on dogs were carried out by the authors with a view to studying the effects of prolonged refrigeration on wound healing. The nature of the healing process in clean incised wounds of the skin and subcutaneous tissues of the forelimb after cooling to 6°C. for a period of from twenty-four to seventy-two hours was determined. Similar incisions on the opposite limb were used as controls. The healing process was studied by measurements of the tensile strength and by microscopic examination of the wounds at varying intervals. The results showed that during the cooling period there was no reaction on the part of the tissues to the injury inflicted by the incision, but subsequently there was a definite delay in the healing of the wounds, the degree of delay varying with the duration of the cooling period. In wounds treated by delayed suture after cooling for from twenty-four to forty-eight hours the incidence of infection is much greater than in control incisions maintained at normal temperatures.

The results of the authors' experiments indicate that certain harmful effects result from prolonged refrigeration of living tissue such as is advocated by some for amputation of gangrenous-infected extremities. It may be held that as the clinical cooling period is often much shorter than the cooling period in these experiments the results are not comparable. Since it has been shown that the harmful effects are proportional to the duration of the cooling period, it may be assumed that some degree of harm must result whenever living tissues are cooled to low temperatures. Therefore it is believed by the authors that refrigeration anesthesia is not ideal for amputations. If the aim is to diminish absorption from a gangrenous region by local cooling this can be accomplished by refrigerating the limb below the desired amputation level in order that the anesthesia so induced will permit the application of a tight tourniquet. After restorative measures have been effective amputation can be carried out under ordinary anesthesia above the level of cooling without harmful sequelae.

Suggestions have recently been advanced that wounds of the extremities which have been incurred on the battle field should be refrigerated during transportation and until proper emergency surgical treatment can be instituted, an interval of many hours or even days. The authors' experiments dealing with the effect of prolonged cooling on wounds treated by delayed or secondary suture fairly closely approximate such war conditions, and because of the increased incidence of wound infection after the cooling period in these experiments, it is recommended that wounds sustained on the battle field should not be treated by refrigeration unless there is no hope of saving the part.

JOSEPH K. NARAT, M.D.

Brunessu, J., and Heinbecker P: The Effects of Cooling on Experimentally Infected Tissues. *Ann. Surg.* 944, 20 7 6.

The effects of reduced temperatures on tissue survival under anoxia and on tissue resistance to infection have been the subject of several recent investigations. The authors report their results of an investigation to determine the effects of reduced temperatures on both the local tissue response and the organisms responsible for it and to determine the eventual course of a local infection as altered by a temporary period of cooling. A concentrated suspension of the streptococcus hemolyticus in broth was used to produce a localized infection in dogs. Cooling was effected by immersing the limb to a level well above the elbow in a constant temperature bath provided by a commercial cooler. The experiments were carried out for periods ranging from twenty-four to ninety-six hours.

The authors concluded from their experiments that as long as cooling to 6°C. is maintained, the subcutaneous tissues of the dog fail to show the inflammatory response usually initiated by the inoculation of the streptococcus hemolyticus. The number of organisms present in the tissues remains remarkably constant and closely approximates the number injected.

The development of extensive subcutaneous edema during cooling and after removal of the cold, and the development of a more marked inflammatory reaction, with a decrease in the growth restricting power of the tissues to bacterial organisms, suggest the possibility of harmful effects from prolonged refrigeration. The effects of cooling are manifest in the deeper as well as in the superficial tissues of the limb of a dog with an intact blood supply.

From these experimental data, it seems evident that the clinical application of cold (6°C.) to infected tissue will have no therapeutic value in itself. Under certain circumstances it may not be harmful to cool an infected limb for a brief period in order to maintain the relative status quo observed in these experiments in regard to bacterial activity and to tissue response. However cooling for longer periods of time (from twenty-four to ninety-six hours) in the authors' experiments resulted in definite changes in tissue hydration, marked vasodilatation, and a de-

crease in the growth-restricting action of the tissues toward bacterial organisms. Moreover these changes became more marked as the period of refrigeration was prolonged. While the exact clinical limitations of the procedure remain to be determined the findings so far would contraindicate the cooling to levels around 6 C. of infected limbs which one aims to save by conservative measures, except for brief periods of time.

JOSEPH E. NARAT M.D.

Ham, A. W.: Experimental Study of the Histopathology of Burns, with Particular Reference to Sites of Fluid Loss in Burns of Different Depth. *Ann Surg*, 1944, 120 689.

The pathology of burns was studied in relation to the blood supply of the skin, because of the importance of the problem of local fluid loss from blood vessels in burns. The pig was selected as the experimental animal since its skin more closely resembles human skin than does the skin of other laboratory animals. Burns of the three degrees were produced in different animals by controlled methods of contact with heat. Grossly the burns produced as a result of contact of shorter duration were characterized by redness of the skin while those due to longer exposure appeared white. The depth of burning is indicated by the resistance of the hairs to being pulled out in deeper burns, fluid that escapes from the capillaries loosens the attachment of the hairs.

A histological study of first-degree burns showed dilatation and congestion of the superficial plexuses of capillaries and venules. (These vessels are the ones concerned in the dissemination of heat.) More severe first-degree burns cause an escape of fluid from these vessels, which may lift the epidermis from the dermis to form small blisters. In these studies all blisters were situated between the epidermis and the dermis.

In mild second-degree burns many of the superficial vessels continue to function and leak fluid. In severe second-degree or white burns the whole superficial group of vessels is sealed off by heat. Although the underlying dermis contains few capillaries much fluid is lost in this type of burn from the intense congestion and dilatation of the capillary beds about the deep secreting portions of the sweat glands and the deepest parts of the hair follicles. It is this escape of fluid that loosens the hair attachments. Fluid lost from this part of the capillary bed readily finds its way to the subcutaneous tissue and it appears that the subcutaneous accumulation of fluid in this type of burn has its origin in the skin.

In very severe second-degree and in third-degree burns, fluid loss actually occurs from the capillaries of the subcutaneous tissue since marked congestion of these vessels with perivascular accumulation of fluid is apparent histologically.

Experiments in which trypan blue was injected intravenously confirmed the histological findings. This dye does not ordinarily escape from the capillary bed fast enough to produce intense diffuse

staining of the tissues. However when plasma escapes into the tissues following burns the presence of trypan blue in the plasma stains the areas of accumulation a deep blue.

These studies also indicated that there are two capillary beds in the skin and one in the subcutaneous tissues which are the chief sites of fluid loss in burns of different intensities. JOHN L. LINQUIST M.D.

Ham, A. W. Experimental Study of the Tannic Acid Treatment of Burns, with Particular Reference to Its Effect on Local Fluid Loss and Healing. *Ann Surg* 1944, 120 698.

An experimental study was made to determine the effectiveness of tannic acid treatment of burns in limiting local fluid loss and its efficiency in this respect with burns of varying degree. Young hogs were used as experimental animals because of the similarities of hog and human skin. Burns of varying degree and the subsequent tanning were produced by controlled methods following which sections of the skin were prepared for histological examination. Epidermis was found to be a barrier to the penetration of the tanning agent so that it was necessary to remove the epidermis with a sharp scalpel before application of the tannic acid.

When tannic acid is applied in successive coats to a burned surface denuded of epidermis it penetrates remarkably evenly into the dermis presumably by combining with collagen in much the same fashion that it does in the manufacture of leather. The depth of penetration depends upon the length of time that the surface is kept wet with tannic acid. Many hours of exposure resulted in a penetration of a quarter up to a third of the thickness of the dermis. Combining with the collagen is not the only effect of tannic acid on the dermis. It also kills viable elements in the dermis for a considerable distance below the layer that is frankly tanned and results in a gathering of leucocytes along a line beneath this dead layer. Both layers separate off in the eschar at the line of leucocytic concentration.

Since it has been shown that the chief fluid loss in first-degree and in mild second-degree burns occurs from the superficial plexuses of capillaries tanning of the surface would tend to prevent this loss. In deeper burns however it has been shown that the fluid loss occurs from the capillaries about the deeper portions of the sweat glands and hair follicles at a level that is not reached by the tannic acid. Tanning could not be expected to diminish fluid loss from these deeper burns in the same direct way that it does so in more superficial burns. Experiments with trypan blue given intravenously showed that keeping the tanned or even untanned surface of the burned area dry was efficacious in preventing trypan blue leakage from a first-degree or mild second degree burn. In deeper burns tanning was found to exert little or no effect on the amount of trypan blue that escaped at the burn site.

Tanning necessarily slows the healing of a very superficial burn in which the complete thickness of

May, 1945

International Abstract of Surgery

*Supplementary to
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INTERNATIONAL ABSTRACT OF SURGERY

VOLUME 80

MAY, 1945

NUMBER 5

THE TREATMENT OF ACUTE AND CHRONIC PROTEIN DEFICIENCIES

Collective Review

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IN a recent communication (24) the subject of hypoproteinemia was extensively reviewed and discussed. The conclusions arrived at can be summarized as follows:

The role of the proteins or their derivatives (amino acids, peptides and others) in the human economy is of paramount importance. Besides being the most important structural constituent of all of the body tissues, proteins enter into part or all of the structure of the various enzymes (pepsin, trypsin, and others) hormones (insulin pituitary and parathyroid hormones, and others), and the various antibodies (modified serumglobulins).

During conditions of health and illness, the protein metabolic function and its daily regulation depends primarily upon good liver function. Normally the plasma protein level of the blood bears an approximately constant relationship to the fixed tissue protein supplies in the body and both of these are guarded against ordinary and excessive demands by the large hidden reserve supplies of protein in the various organs and tissues of the body.

Protein replacement in general takes place from ingested food. Plasma proteins are renewed constantly from the reserve stores of plasma protein building material as well as from newly ingested amino acids. Not only the quantity but also the quality of the food proteins is of the utmost importance in the production and regeneration of the various plasma and tissue proteins.

In the light of present evidence it would seem that plasma, tissue, and reserve proteins do not remain static after being elaborated, but rather participate in a dynamic equilibrium as suggested by Madden and Whipple (12) and that the nor-

mal balance results from the continuous ebb and flow between the old and the new in the continuation of the normal metabolic activity.

The food supply of protein furnishes the material for the regeneration of all of the protein fractions in the total plasma protein—albumin globulins, fibrinogen, and prothrombin. After the amino acids (resulting from the hydrolytic digestion of the food protein) reach the liver by the portal vein, they are built partly into proteins and partly into plasma protein building material. A portion of this synthesized material is placed in the reserve store of proteins. In these reserves are placed the precursors of the plasma proteins, although a portion is stored as fully formed protein which is then available instantly in times of stress. It is apparent, therefore, that the cycle of plasma protein formation revolves around the liver both from the viewpoint of formation and from that of storage.

PLASMA PROTEIN DETERMINATIONS

The presence of continued low plasma protein concentrations should be taken as a clinical indication of a profound nutritional disturbance and of a general metabolic deficiency disease. This may be a primary condition, or may be secondary to serious disease especially of the liver parenchyma. Any manifestation may, therefore, be either the cause or the result of this abnormality and commonly both of these effects become intertwined clinically. Specifically this has special reference to the albumin and globulin fractions of the total plasma protein in general cases of hypoproteinemia (undernutrition) and to the fibrinogen and prothrombin fractions in sharply defined

activities relating to the blood clotting materials and function.

The importance of plasma protein estimations for clinical purposes lies in the fact that they can be measured. In making these determinations, however one must take account of any accompanying state of dehydration or hemoconcentration as this tends to give abnormally high values, or of any state of excessive blood hydration which would decrease the relative total serum protein content. Estimations of the total plasma protein concentration in the blood may not indicate the true status inasmuch as a diminution of the serum albumin fraction may coexist with a corresponding increase of the serum globulin fraction. For this reason, blood-volume and albumin-globulin-partition studies are necessary in each case because the total plasma protein contents may not be correctly indicated by the concentration per unit measure of blood. In any event, plasma changes are clinically demonstrable only when the reserve supplies of protein are sufficiently compromised. In general, the amino-acid content of the tissues is about ten times as great as that of the blood plasma. We do not have accurate knowledge of what proportion the hidden reserves of protein-building material bear to either one of the latter. But it must be very large indeed because changes in total serum protein do not occur until the body weight is appreciably compromised, except after severe hemorrhage, traumatic shock, burns, and so on.

In clinical practice a single determination is not of much value. However a succession of repeated observations is immensely valuable because it reveals the course of the disturbance through the deterioration or improvement, primarily, of the protein function and secondarily of any liver cell damage. When repeated in a series, quantitative estimations of any protein deficiencies, and their progression or retrogression, give valuable information concerning the state of function of the liver parenchymal cell or of the deficiency in general and enable fairly accurate prognostications. So that when the deterioration of function, as indicated by the repeated tests, indicates a progressive diminution or when the grade of deficiency is very extreme, these laboratory determinations act as important criteria for determining the immediate advisability of any contemplated operation, the choice of an anesthetic, or the method of operative procedure. In some cases, they suggest efforts to improve the disabling factor and operation must then be postponed until the disability is removed or sufficiently improved. In still other cases, they establish the irreversibility of the

already existing damage, and, when this is sufficiently far advanced they contraindicate conclusively any operation of an elective nature.

In a general way the laboratory demonstration of hypoproteinemic states with or without a coincident loss of body weight indicates some interference with liver cell function. But inasmuch as the method of production of this deficiency varies, there can be no assumption of intrinsic liver disease, except as it corroborates one's diagnosis on other more appropriate and reliable criteria. Nevertheless, even for this purpose, repeated determinations are valuable as corroborating proofs of liver cell damage, when all other clinical and laboratory findings point definitely to the liver as the essential seat of the disease, and, to a lesser extent, when latent disease is suspected.

CLASSIFICATION OF HYPOPROTEINEMIAS

In accordance with the basic production mechanism of hypoproteinemia, one can distinguish three types (Davis and Getsoff 5) of this general protein deficiency:

1. Hypoproteinemia of the prehepatic type which is caused by interference with adequate nutrition intake, digestion, or absorption of plasma protein-building materials, without any disturbance of the ability of the liver to form plasma proteins as the supply of protein-building material is inadequate. This is the most general and important cause of hypoproteinemia.

2. Hypoproteinemia of the hepatic type, which results from the inability of the liver itself to build plasma proteins, despite the fact that adequate supplies of plasma protein-building material are received. In most of the reported cases, this is accompanied by other evidences of a reduction of liver function in the presence of apparent liver disease. A similar effect is demonstrable in latent hepatic disease also.

3. In the posthepatic hypoproteinemia, there is an adequate formation of plasma proteins by the liver but an abnormal amount of plasma proteins is lost, for example, (a) in repeated bouts of, or in a severe, diarrhea (b) in excessive albuminurias (nephroses) (c) following a large hemorrhage (d) accompanying any outpouring of serum in any hollow cavity (pleural effusion peritoneal ascites, or peritoneal exudation) and (e) following the exudation of serum in large traumatic areas (burns). This form is often combined with under nutrition (group 1).

CLINICAL DISTRIBUTION OF HYPOPROTEINEMIA

Various grades of hypoproteinemia have been clinically observed in many abnormal states and

in many forms of disease. In undernourished and otherwise apparently healthy individuals, the protein reserves become dissipated and exist at abnormally low levels without any subjective or objective manifestations. The compensatory mechanism is sufficient to make good the ordinary wear and tear of the tissues up to a certain point and there may be no laboratory or other method of determining the state of the protein reserves. However upon the appearance of any undue strain—illness, anesthesia operation—this deficiency may become clinically perceptible, and frequently be demonstrable by laboratory means if it is not already apparent clinically.

Hypoproteinemia of this (prehepatic) type occurs in periods of famine (in India China) during wars (the first World War) as a consequence of individual whims in dieting (vegetable diets and so on) in alcoholics, often in pregnant women who do not take sufficient nourishment, and both before and after operation in malnourished individuals.

In industrial practice. Fatigue is, probably the most important form and cause of disability in the industrial worker. It is an important factor because it spells decreased and/or faulty production either for the individual himself or because of his deficiencies, for his fellow workers when he is engaged in team work. Any extraordinary form of fatigue or its undue prolongation should immediately arouse suspicion that some underlying disturbance is present. Two factors operate to bring this situation about (1) sufficiently severe malnutrition and (2) any form of latent disease especially of the liver. Under these conditions a state of protein deficiency and hypoproteinemia results, the symptoms of which include (1) loss of weight and strength (2) loss of stamina or pep (3) various degrees of chronic fatigue (4) a much lessened resistance to other varieties of infections and disease and (5) deficient healing power in any industrial and/or other trauma. At the same time these symptoms are the earliest manifestations of latent hepatic disease. In many cases all of these factors became involved in a vicious circle and the one aids abets and intensifies the others and their effects.

Any industrial worker showing any of these manifestations should immediately be examined for any possible state of protein deficiency or hypoproteinemia, and for the possible presence of any associated latent liver disease.

In military practice. No matter how well soldiers are fed behind the front lines, nutrition is very apt to deteriorate under combat conditions. Frequently the men are under "starvation" condi-

tions. There is decreased general resistance to any extraordinary episode or trauma, and the general condition is not what an active soldier should possess. In previous wars, the healing of wounds was notoriously behind that seen in civil practice. There is loss of weight and protein deficiencies are undoubtedly common. The fact that plasma transfusions have done such wonders for the wounded in this war only goes to show that plasma furnishes much ready protein for the injured soldier. Acute protein deficiencies are a feature of the extensive burns which present battle practice and methods have caused to a much larger extent than any previous war. It is to be remembered how important an enriched protein diet is for all the wounded otherwise disabled and convalescing soldiers in all evacuation and home hospitals.

In traumatic conditions. Acute and subacute protein deficiencies occur in association with extensive traumatic conditions large suppurating wounds, severe infections, and especially burns. In the latter the protein deficiency corresponds to the extent of the burned area and when the latter is large, the protein loss attains extraordinary amounts.

Nutritional edema. Occasionally one sees patients who have general (subcutaneous serous cavity) edema without evidence of the usual forms of pathology which produce such waterlogging. They have no elicitable manifestations pointing to nephritis hypertension cardiac disease cirrhosis myxedema or a malignant growth.

We have come to know that these patients have moderate or excessive degrees of hypoproteinemia sometimes as low as 4.5 gm. per cent of total serum protein. There is reason to believe that an underlying liver parenchymal disease is present and they improve when adequate supplies of protein are provided. For want of a better name their condition has been included under the general term of "nutritional edema."

Starling ('0) was the first to call attention to the part played by the osmotic pressure of serum proteins in regulating the interchange of fluid between the blood stream and the tissues.

The Starling hypothesis has helped to explain these clinical conditions. Sufficient available protein helps to maintain a normal colloidal osmotic pressure in the blood stream and in the capillary bed. Protein deficiencies are now thought to disturb the physicochemical conditions to the extent that water is retained in the body tissues with the formation of edematous areas and in the hollow spaces with the accumulation of edema fluid. This change causes more or less reduction in the amount of urine secreted, causes states of hemoco-

tion, and facilitates pseudo-obstructive manifestations. Nutritional edema and the otherwise obscure accumulations of fluid in the hollow spaces and cavities are only understood on this basis.

Occasionally similar forms of general edema occur when the total serum protein level is apparently in the normal range. In these seemingly paradoxical cases, it is found that the albumin concentration is low and that the globulin concentrations are increased, that because the osmotic pressure of the globulin fraction is much lower than that of the albumin fraction, there is a lower total osmotic pressure and that this disturbed physicochemical relationship permits fluid to accumulate in the tissues and hollow spaces.

Hypoproteinemia with other differentiated forms of disease. In clinically established disease, protein deficiency including lessening of the normal reserve occurs in any basic condition of undernourishment (from insufficient diet to actual starvation, in prolonged vomiting and so on) in any condition associated with loss of digestive capacity (disease of the stomach, pancreas) in any condition associated with decreased intestinal absorption with or without increased alimentary-tract elimination (the various diarrheas and dysenteries).

Hypoproteinemic states are found in all varieties of established or latent liver diseases (atrophic and hypertrophic cirrhosis, the various forms of acute and subacute yellow atrophy, biliary cholelithiasis, acute and chronic cholangitis in gross and capillary forms) after burns of the body in luetic, tuberculous, and malignant disease of the liver, in all forms of traumatic, toxic, and/or chemical injury of the liver and in the destruction accompanying liver suppuration (Johansen, 11; Thompson, McQuarrie, and Bell, 21; Casten, Bodenheimer and Barham, 3).

In severe thyrotoxic disease, two factors operate to produce protein deficiency (1) an associated parenchymal lesion in the liver and (2) the increased catabolism of protein due to the generally increased metabolic activity as shown by the high metabolic rate. The importance of this is becoming more and more generally known.

Protein deficiency also occurs in renal conditions (nephroses) in which albuminuria is an important factor. In certain severe conditions accompanied by excessive loss of nitrogen due to abnormal destruction of tissue, there are large losses of nitrogen in the urinary output, and the tissue and reserve stores of protein become abnormally depleted. Frequently too, this loss is enhanced by the inability to take and absorb nutrition for replacement purposes. Protein deficiency is also found in the malnutrition accompanying

the wasting of any chronic disease (malignancy, tuberculosis) and very often in association with various grades of anemia.¹

POSTOPERATIVE HYPOPROTEINEMIA

A state of negative nitrogen balance exists for varying periods after operation. The important factors include (1) anesthesia (2) a major surgical procedure with operative manipulation of deeply situated viscera and tissues (3) a brief period of starvation (4) shock, fever, vomiting, and the presence of injured tissues. In addition, Cuthbertson (4) has demonstrated appreciable losses of nitrogen after severe and extensive operations as well as after severe injuries. There seemed to be no correlation between age, sex, the presence or absence of malignant neoplasm or other type of disease, and the extent of nitrogen loss.

The adverse effect of general and spinal anesthesia upon the liver cell seems to be increased in hypoproteinemic states, and by the preoperative and postoperative use of drugs of the sulfanilamide group which also have the tendency to increase any destructive effect upon the liver cell.

Various studies have indicated that pulmonary complications occur much more frequently in elderly malnourished subjects than in others. In these persons the usual hypoproteinemias which occur and are expected after severe abdominal operations seem much more increased.

The major portion of the protein loss occurs during the first four or five days after operation during which time food is not permitted at all, or only in limited quantities and, ordinarily, this seems to be the most important factor. Since this brief period of protein deprivation or limitation is well tolerated, the vast majority of patients recover without any special attention to the temporary abnormality of the nitrogen balance, and the hypoproteinemia is made good directly after the return to full diet. However the diet must contain not only protein but also carbohydrate and fat, as nitrogen equilibrium cannot ordinarily be achieved on a pure protein diet.

POSTOPERATIVE ASTHENIA

Quite commonly it has been clinically noted that following major surgical operations of various types, there is frequently a rather prolonged asthenia which is often appreciable for a few

¹There are certain congenital malfunctions of the protein metabolism in which the deficiency is not reflected or recognized in any demonstrable anatomical pathology. The subjects are in apparent good health and the only evidence of any such disorder is an increased secretion of an abnormal urinary constituent, usually an intermediate product in the metabolism of particular body substances. These congenital deficiencies of the protein metabolism, known clinically as cystinosis, alcaptonuria, phenylketonuria, and tyrosinemia, have no relation essentially to the subject under discussion.

weeks or even longer after discharge from the hospital. Leriche has referred to this syndrome which cannot be clearly defined as "maladie postopératoire," and ascribed it to generalized disturbances of the sympathetic nervous system. This form of asthenia has been encountered, perhaps, most often after operation upon the pancreas—pancreatic asthenia (Whipple 23)—and less often upon the gall bladder and liver or after severe destructive disease. Not enough is known concerning all of these forms of postoperative asthenia, and further investigation is necessary. But it is interesting to speculate upon the possible role of any postoperative nitrogen loss in this connection. While the quantity of tissue protein lost may not be large, the source and character of the catabolized protein under these conditions are not known and might conceivably differ from those of the stores depleted. A general hypoproteinemia may result, or there may be a loss of certain reserve protein fractions or of necessary preceding amino acids, when in the course of their usual activities the subjects simply refrain from their customary protein foods and nevertheless continue their normal activities.

Multiplicity and combinations of causal agents and conditions. In many cases, both surgical and medical, more than one cause for the hypoproteinemia is present. There are often associated anemia and avitaminoses.

THE TREATMENT OF CLINICAL HYPOPROTEINEMIA

The preventive treatment of hypoproteinemic states depends to a great degree upon the cause of the deficiency and upon the method of its production. In ordinary states of undernutrition, the essential of therapy is increased and abundant nourishment. In disease of the gastrointestinal tract, this must be combined with rectification of the underlying disease, either an increase of the digestive action or an elimination of abnormally increased bowel evacuations. In hemorrhage, replacement of the lost blood is imperative. In essential disease and/or injury of the liver parenchyma, removal of the cause (chemical or other poisoning, deficient food with and without deficient vitamin supply) must be accomplished. In thyrotoxic disease, lowering of the basal metabolic rate with drugs (iodine, thiouracil and others) or by subtotal thyroidectomy with or without preceding medication is necessary. In renal nephroses and albuminurias, the kidney condition must be improved, and so on. In mild states of hypoproteinemia, these measures including the proper additional supply of protein foods by mouth will suffice.

In operative cases the assurance of an adequate supply of protein is most important first to protect the liver from the possible toxic effects of anesthesia, second, to prevent tissue edema, which interferes with healing of the wound, and, third, to supply the essential nutrients required for tissue repair and regeneration.

The emphasis which has been placed on correcting dehydration and electrolyte losses before and after operation has often been accompanied by failure to consider the mechanism involved in keeping fluids in the blood vessels (Starling hypothesis). Proper control of the fluid and electrolyte balance in surgical patients receiving parenteral fluids is not possible unless the serum-protein concentration is maintained within normal limits.

If no success follows in the mild cases or it follows in insufficient degree if the grade of the protein deficiency is severe or extreme, or if there is any necessity for urgency in the correction of the hypoproteinemic state, more active measures are necessary including the parenteral replacement of protein. Parenteral replacement of protein can be accomplished by (1) the transfusion of fresh whole blood, (2) the transfusion of wet or dried human plasma, (3) the reinfusion of human transudate fluid (ascitic and/or pleural), and (4) the use of amino acids.

All of these have their distinct place and field of usefulness in therapy and each, or a combination of them, should be selected in any individual case in accordance with the purpose to be accomplished. In any case, an estimation of the good effect which is being accomplished can be obtained from a laboratory standpoint by estimations of the total protein content of the blood plasma and, clinically by evidences of improvement in the general condition of the patient and of any local (operative, traumatic) condition which is present.

1 AND 2. TRANSFUSIONS OF WHOLE BLOOD AND/OR PLASMA

In emergency conditions and/or in any immediate postoperative period transfusions of blood are the most satisfactory method for restoring the protein supply both because of the ease of introduction and because of the rapidity with which results are obtained. Under nonemergency conditions, and in long-standing conditions in which protein replacement therapy must be carried out continuously and for long periods of time, such transfusions are not practicable, except under unusual conditions, both because the supply of blood is necessarily limited and for reasons of cost. When the need for red cells does not exist, excessive whole-blood transfusion can be dangerous

since it may lead to seriously elevated hematocrit values.

When whole blood is, for any reason, not available human plasma forms a most excellent substitute and approaches practically completely fresh whole blood even though at present it suffers from the temporary disadvantages of expense and inadequacy of supply. About 1,000 cc. of plasma are required to raise the protein content of the plasma of the average adult 1 gm. per 100 cc. In severe hypoproteinemia many liters of plasma may be needed. When plasma is given, absorption and synthesis are unnecessary. After liver injuries, burns, and so on plasma transfusions have proved to be life saving.

3 THE REINFUSION OF HUMAN TRANSUDATE FLUID

In the hypoproteinemia accompanying the cirrhoses with ascites, or in nutritional edemas, human transudates may be used. Remarkable results have been obtained the plasma proteins become elevated great diuresis follows and the ascitic fluid may not reform for quite a long time.

The available transudates which can be used are those in the abdomen and those in the pleural cavity. The latter are much the richer in protein content, sometimes averaging as much as 4.5 per cent. ascitic fluid usually contains between 1 and 2.5 per cent, occasionally as much as 4 per cent. Ascitic fluid is usually more abundant. The fluid transudate is obtained by tapping under rigid aseptic control. It is possible and even desirable to pool fluids from more than one source, as in the use of blood plasma. No grouping or typing is necessary. Before use each batch of fluid should be tested bacteriologically and any excess complement can be eliminated by heating the fluid in water both to a temperature of 56° C. for fifteen minutes.

In nutritional edemas and similar conditions, the use of transudate fluid seems especially applicable. In any large center of population, and in any large hospital environment there should be numerous opportunities for securing such fluid in relatively large quantities. The fluid is easily manipulated, no tests are necessary and there is a minimum of danger and little or no reaction.

I know of one case (Simons, 19) in which this method was repeatedly employed for a year or more without temperature or other reaction at any time.

4 THE ADMINISTRATION OF PROPERLY PREPARED AMINO ACIDS (HYDROLYZED CASEIN AND SO FORTH)

Amino acids can keep the body in nitrogen balance, and are much more economical and more

easily obtainable than plasma. Amino acids require no further digestion and are available to the cells immediately after they enter the blood stream.

When protein is eaten it is hydrolyzed into polypeptides and into amino acids of the general formula $R-CH(NH_2)COOH$ by the proteolytic enzymes, pepsin, trypsin and erepsin. The process is very complex. The final digestion of protein takes place in the small intestine and the resulting amino acids and small peptides (?) pass into the blood stream and are circulated throughout the body. Various cells in the body then take up the amino acids and peptides for the synthesis of nitrogen-containing products into proteins and protein-building material.

The usual human diet contains varying amounts of protein from animal and vegetable sources. The nutritive value of any of these depends upon its digestibility its potential amino-acid content, and its content of those individual amino acids (valine and methionine) which have been proved indispensable. The known amino acids are

A. Essential	B. Nonessential
1. Lysine	1. Glycine
2. Tryptophane	2. Alanine
3. Histidine	3. Serine
4. Phenylalanine	4. Norleucine
5. Leucine	5. Aspartic acid
6. Isoleucine	6. Diisotyroline
7. Threonine	7. Proline
8. Methionine	8. Hydroxyproline
9. Valine	9. Thyroxine
10. Arginine	10. Tyrosine
	11. Glutamic acid
	12. Cystine (cysteine)

The essential amino acids must be present in the dietary protein to assure normal growth for the animal organism. The "nonessential" amino acids either may not be required by the body at all, or may more probably be synthesized by the body from other amino acids (Rose, 17). As yet, however little is known of the quantitative requirements of individual amino acids or the function of each in the body.

Of the amino acids listed in column A above, all but histidine and arginine have been found necessary for the maintenance of nitrogen balance in normal adult males. A deficiency of even one of the amino acids that are essential for tissue construction limits the value of a protein to the animal body. A number of the proteins occurring in foods are deficient in one or more of the essential amino acids.

For example, diets which consist mostly of milk are insufficient for maintenance as shown by bed-

ade experience in postoperative cases, while gelatin, although rich in glycine (an amino acid that may be synthesized by the body) does not contain tryptophane and valine (essential amino acids) nor tyrosine which is nonessential. The amino acids in fish and meat measure up very favorably with the as yet unknown requirements for normal maintenance and growth. Generally speaking animal proteins contain all or nearly all of the essential amino acids, but vegetable proteins do not. However one can obtain similar end-results and effects by supplementing the various vegetable proteins with one another, and with or without the supplementation of an amino-acid mixture until the total amount is adequate. Under such circumstances, animal proteins are not absolutely necessary. Customarily however human beings prefer a diet containing a large amount (more than half) of the protein from animal sources. In any case, the plasma proteins can be synthesized only if the body receives the proper mixtures of amino acids.

In any condition in which surgical shock is a factor amino acids¹ find no place because they are foods and when they are injected into the circulation they are taken up quickly by the body cells and removed from the blood stream. Under such conditions, blood and plasma are preferable, because they stay in the circulating blood and raise the osmotic pressure and the volume of the blood.

The administration of amino acids is especially indicated when the need for replacement protein therapy extends over an appreciable length of time: less frequently as an exclusive means and very much more frequently as an adjuvant method in addition to the ordinary food intake of the individual. Here the oral administration of amino acids finds its special field.

a. The administration of amino acids by the oral route. It has been shown conclusively that a mixture containing all the essential amino acids can be given orally that, when so administered, the amino acids are rapidly absorbed from the gastrointestinal tract that in this manner they may be substituted for food protein that by this means a patient may be kept in nitrogenous equilibrium and that no untoward effects occur or follow. If such a mixture is given in relatively large quantities, however it is sometimes irritating.

b. The administration of amino acids by the intravenous route. The possibility of supplying protein parenterally with amino acids was done

experimentally as early as 1913 by Henriques and Andersen (10) and has since been suggested for clinical use by others, particularly by Rose (16) in 1934.

The intravenous administration of amino acids has been employed by Elman (6, 7) Farr and MacFadyen (8) Shohl and associates (18) Whipple and associates (22) by myself, and by others. Theoretically the method is good, but it presents several practical difficulties, not the least of which is the preparation of a standardized hydrolysate which is safe for intravenous use.

The earlier difficulties have largely disappeared with successive improvements in the manufacture of a proper hydrolyzed casein which so far has been found to be the best source of material. The solubility has increased so that a perfectly clear solution can be administered intravenously with minimum danger of phlebitis when long periods of venoclysis are required. However this danger in any case is not very great with the dilute (2 per cent) solutions.

The most serious difficulty has proved to be the occurrence of occasional febrile reactions (Shohl, 17 Elman 6 and others).

Untoward reactions are due to one or more factors connected with the manufacture of the hydrolyzed casein, with its method of solution and preparation for intravenous use, or with the technique, i. e. the rapidity of the administration itself. Nevertheless, the preparations now available have been administered to many patients without untoward effects by myself and by other observers.

In the experience of Brunschwig, Clark, and Corbin (2) minor disturbances were frequent they included anorexia, mild and occasionally severe nausea and vomiting and a generalized disagreeable flushing sensation. In the exceptional instances these were sufficiently pronounced to warrant discontinuation of the injections after one or several attempts.

It would appear that in certain types of acute hepatitis, a sudden flooding of the circulation with amino acids is too great a physiological load for the liver to tolerate. Nevertheless, postmortem studies of 9 patients who received substantial quantities of casein digest during their terminal disease failed to reveal evidence of toxic effects ascribable to the digesta.

c. The administration of amino acids into the bone marrow. Solutions of amino acids are found to be equally effective when injected into the bone marrow. This method offers a satisfactory way of achieving parenteral injection when the other routes are inaccessible, impossible, or inadvisable.

¹The expensive amino acids will be used here in the sense of soluble mixture of amino acids and other protein-split products derived from the by analytic solution of proteins.

The injection of amino acids into the bone marrow was done intrasternally by Altschuler, Sahyun, Schneider and Satriano (1) with Turkel needles, and it was found that amino acids may be given by this route as rapidly and in as large an amount as by the intravenous route. The results were no different than those with the other methods, but intrasternal administration was advantageous in patients in whom access to the veins was difficult. The Turkel needles may be left in place for twenty four hours or longer and repeated injections may be given through them.

General considerations in intravenous and in intrasternal administration of amino acids. In various conditions patients are able to metabolize from 5 to 30 gm. of protein in the form of amino acids¹ per hour. The average patient is able to take up to 15 gm. per hour and when this is properly given about 95 per cent of it is utilizable. The solution should not be administered any more rapidly than the subject can metabolize it. In order to supply enough carbohydrate simultaneously it is usual and best to give the amino acids in a 5 per cent solution of glucose, either alone or in saline solution. Glucose is usually metabolized at the rate of 0.84 gm. per hour or kilogram of body weight, according to most authorities. Usually large quantities of both amino acids and glucose are required if any good is to be accomplished.

When the paradoxical observation is made that protein concentration is decreasing while the hemoglobin is increasing as fluids are given intravenously one should deduce that plasma is being lost from the blood stream. According to Minot and Blalock (15) the indication, then, is to give increasing amounts of protein, possibly with colloids to increase the osmotic pressure. Very large amounts are needed.

d. Administration of amino acids by the subcutaneous route. When intravenous amino acid is not well tolerated, a 3.3 per cent solution in distilled water may be given safely by hypodermoclysis without discomfort and reaction in the tissues. Patients with clinical icterus, or toxic forms of marked liver damage, as shown by functional tests, commonly have reactions after intravenous injection, but they tolerate hypodermoclyses of the 3.3 per cent solution well.

e. The administration of amino acids by rectum. This has been reported by Griesbach (8), and by McClendon, Cavett and Johnson (13). However the usefulness of the method is questioned by McLester (14) on the ground that rectal feeding is, at best, limited because of the variabilities of

its absorption. I am inclined to agree with the latter statement.

THE MANAGEMENT OF PROTEIN REPLACEMENT THERAPY

a. General considerations

In a few of the cases with chronic protein deficiency it may be found possible to provide an adequate diet which will give not only enough calories, vitamins, minerals, and protein, but an excess of protein to correct any existing protein deficiency. However, the correction by such methods requires considerable time. This method will find its greatest usefulness in the mildest type of case, in the postoperative period in subnormal subjects, and possibly in the cases of postoperative asthenia.

However even in these cases and certainly in all other cases, it is very advisable to reinforce the high-protein diet with amino acids in order to give a maximum amount of protein-building substances. In any case, enough should be provided, if possible, to give a superabundance and this should be supplemented with sufficient carbohydrates and fat.

It usually is possible to feed enough carbohydrates and fat to meet the caloric requirements, and then provide excess protein nutrition by supplementing such proteins as the patient can eat with sufficient quantities of amino acids administered orally.

The amount of protein (including amino acids) administered should be estimated upon the basis of the difference between the nitrogen intake and output of the individual. The amount of total circulating protein is calculated by multiplying the plasma volume by the protein concentration. The amount of other body protein (tissue and reserve protein) is usually estimated to be 30 times the plasma protein. The total nitrogen excretion per day in urine plus feces multiplied by 6.25 will give approximately the amount of protein broken down in the body during the twenty-four hour period.

An intake of protein or amino acids equivalent to the protein destroyed in the body will suffice to keep the body in nitrogen balance, but it will not allow for correction of the tissue protein deficiency or for the raising of the plasma protein level. An additional amount over that required for balance must be given if protein deficiency is to be corrected. Probably the greater the excess, the more rapidly and more efficiently the correction of the deficiency takes place.

The number of calories any one person requires for twenty-four hours for various activities can be

¹One gram *N* equals 6.25 gm. protein.

CHART I.—THE FOOD MINERAL, AND VITAMIN REQUIREMENTS OF AN INDIVIDUAL

(This chart is taken from the recommendations of the Committee on Foods and Nutrition of the National Research Council.)

	Cal- ories	Total Calories Daily Derived from		Cal- cium gm.	Iron mgm.	Vita- min A+ I U	Thia- min mgm.	Ascor- bic Acid mgm.	Ribo- flavin mgm.	Nia- cin mgm.	Vita- min D I U
		Protein	Carbo- hydrate and Fat								
Man (70 kgm.)											
Fully active	3000	240 (70 gm.)	2,760	0.8		5000	1.8	75	2.7	18	
Very active	4500	240 (70 gm.)	4,100				2.3		2.3	23	
Sedentary	2000	240 (70 gm.)	2,760				1.2		2.3	5	
Woman (60 kgm.)											
Fully active	3000	240 (60 gm.)	2,760	0.8		5000	1.5	70	2.7	15	
Very active	3000	240 (60 gm.)	2,760				1.5		2.7	15	
Sedentary	2000	240 (60 gm.)	2,760				1.2		2.7	15	
Pregnancy (latter half)	3000	340 (85 gm.)	2,420	1.5	5	6000	1.5	00	5	18	400-800
Lactation	3000	400 (100 gm.)	2,600	2.0		8000	2.3	30	5	23	400-800
Children 1 to 12 years											
Under 1 year	1000*	3-15 (3-4 gm.)	84*	1.0	6	500	4	30	0.6	4	400-800
1 to 3 years	1000	150 (40 gm.)	1040		7	1000	6	35	0.9	4	
4 to 6 years	1500	200 (50 gm.)	1400		8	1500	8	50	1.3	8	
7 to 9 years	2000	240 (60 gm.)	1760		10	2000	1.0	60	1.9		
10 to 12 years	2500	280 (70 gm.)	2,220	1.5	12	2500	1.2	75	2.3		
Girls											
1-15 years	2500	280 (70 gm.)	2,220	1.5	12	2500	1.2	75	2.3		
16-20 years	2500	280 (70 gm.)	2,220	1.5	12	2500	1.2	75	2.3		
Boys											
1-15 years	2500	280 (70 gm.)	2,220	1.5	12	2500	1.2	75	2.3		
16-20 years	2500	280 (70 gm.)	2,220	1.5	12	2500	1.2	75	2.3		

*Per Kg.

†mgm. Thiamin = 100 I. U.; mgm. ascorbic acid = 10 I. U. (I. U. = U. S. P. unit)

‡Less may be required if provided as vitamins A; greater if chiefly as provitamin carotene

§Infant needs increase from month to month. Ammonia gives are for approximately 16-18 months

¶Amounts of protein and calcium needed are less if from breast milk.

**Vitamin D is not necessary for older children and adults. If not available from sunshine, should be provided probably up to minimal amounts recommended for infants.

††Urverages based on middle age for each group (as 2, 3, 4, etc.) and for moderate activity

‡‡Good formula for the average grown adult would include carbohydrates from 60 to 80 per cent, fat from 5 to 10 per cent, and protein from 30 to 35 per cent plus the necessary vitamins and minerals.

determined with great precision. For a moderately active person, 45 calories per kilogram are adequate for a very active worker 65 calories and for a sedentary worker, 37 calories per kilogram. Soldiers require from 60 to 65 calories. For an active child, the caloric requirement is quite high, and exceeds that of an adult.

The daily protein recommendation for an adult is 1 gm. per kilogram of body weight, i. e., roughly speaking 70 gm. of protein a day for the average man with a body weight of 70 kgm. or 10 per cent of the required 3,000 calories. For children under six years of age, 3 gm. of protein daily per kilogram of body weight are necessary. Children above the age of six should be maintained on 2 1/2 gm. daily per kilogram of body weight until they become adults. Nutritionists, today, are generally agreed that the liberal use of protein in the diet (from 80 to 100 gm. or more, daily) has no deleterious effect either on the kidneys or on the vascular system. On the contrary there is evidence that a high protein diet stimulates vigor and physiological efficiency.

Amino-acids therapy to be effective, must be supplemented with sufficient carbohydrates, fats, minerals, and vitamins, and an abundance of fluid to meet the caloric and all other requirements of the body. Under such conditions, amino acids are free to be manufactured into body proteins. They will do this more effectively if protein food substances are supplied in the diet in addition.

b Protein replacement therapy under specific conditions

With all of these facts in mind, and under proper laboratory estimations of the protein nitrogen balance of the individual, the following rules can be advantageously used under various conditions. As can be seen, the suggestions follow along in the order of intensity of the hypoproteinemia and general protein deficiency. They should be varied as the indication is acute and demands urgency in treatment, as the therapy is necessary to correct a long drawn-out condition as a result of which a chronic hypoproteinemic state has resulted or as the indication arises and either disappears or becomes intensified. It should be understood that

each case is a feeding problem in itself and that the latter gains or loses in importance in accordance with the urgency produced by an advanced state of protein deficiency incident to undernourishment, starvation, or severe gastrointestinal disease by an underlying severe hepatic parenchymatous disease with its resultant nutritional metabolic disturbance or by some extraordinary circumstance, as an operation.

In calculating the daily necessary amount of protein, the following factors must be considered (1) the patient's nitrogen balance (2) the estimated degree of deficiency in the tissue and reserve protein and (3) the possible continuance of the original disability which caused the deficiency if one exists finally an additional amount of protein should be given to allow for any unavoidable error in the computation.

In severe cases one may follow the same rule of thumb that one frequently does with abdominal drainage—whenever in doubt, give more—and in very severe cases one should give as much as possible by every available channel and method up to the limit of tolerance.

In the following conditions, an estimation is made of the daily necessary supply of protein.

In general malnutrition. In early cases of general malnutrition about 2 to 3 times the normal requirement, calculated at the level of 60 calories per kilogram of body weight, should be given. The amount should be increased in accordance with the degree of malnutrition and in advanced stages as much as the patient will tolerate should be given regardless of the calculated estimate.

In anemia. In advanced cases, as much as 25 per cent of the globin protein may be lost. The serum albumin factor seems to be the necessary replacement item. The fact that an anemia is present indicates that the preceding nutritional disturbance has existed for a long time. Hence it is necessary to follow the same rules as in any moderate or advanced case of general malnutrition.

In nephritis and/or nephrosis. The albumin lost daily in the urine is easily calculated. Anywhere from 2 to 3 times the amount lost is necessary to replace the latter and to make good the other factors previously indicated.

In infections. Metabolic activity is so greatly increased during these infections that from 2 to 3 times the normal amount is necessary.

In burns. Losses of one third or more of the plasma are often dissipated daily in very extensive burns. These losses are increased with any added infection or in the presence of high fever. The total catabolic loss may be as high as 250 gm.

per day plus the amount lost by seepage in the burned area. All of these factors are to be taken into account in estimating the necessary replacement supply of protein. But for practical purposes the maximal amount of replacement therapy (anything up to 10 times the normal requirement or the limit of toleration) should be employed and sometimes the amount needed is more than the subject can assimilate.

In alcoholism and in hepatic parenchymatous disease. Both of these can be considered together because the protein replacement therapy for chronic alcoholism is the same as for the prevention of, or the early-stage treatment for parenchymatous disease of the liver.

In all stages the essential disability is that of a severe malnutrition. In moderately advanced and in far advanced conditions, the calculation should include the daily loss of nitrogen, an estimate of the tissue and reserve protein deficiency and a calculation of the amount of protein lost in digestion from the amount administered. Then this should be multiplied several times in order to obtain an exceptionally rich protein diet. In severe cases as much as from 4 to 5 times the calculated normal must be given for a long time before any beneficial result is seen.

In hyperthyroidism. The calculation should include the loss from the extraordinary metabolism due to the disease, plus the deficiency incident to any hepatic parenchymatous disease which is a common complication. The treatment should follow the suggestions given for severe malnutrition plus those for hepatic parenchymatous disease. The nitrogen balance is most important in the calculation but due consideration should be given to the metabolic rate.

In the preoperative preparation of patients with malnutrition and hypoproteinemia. There is here the double nutritional disturbance resulting from (1) the indication for operation (gastrointestinal disease with either vomiting and/or diarrhea, carcinoma, dysenteries, hyperthyroidism, hepatic disease, and so on) and (2) the operation itself.

All grades of malnutrition will be present but as a general rule it is well to add together the protein loss present, and to be anticipated in the post-operative period plus an added increment for good measure. If the time available for this preparation is limited, the most strenuous methods (blood, plasma, and/or albumin transfusion) should be employed and the amounts given should be increased.

In the postoperative period. For those patients whose operations are necessitated by conditions unassociated with protein deficiencies, no particu-

lar protein replacement should be done as these subjects accumulate and replace any lost protein as soon as they are back on a normal, or somewhat richer normal diet.

In all other patients, in accordance with the degree of the deficiency the length of time it has existed, the nature of the operation, and so on the deficiency should be calculated and replaced as in the preoperative preparation, of which the post operative therapy is only a continuation with some intensification of the program.

In industrial practice. Physicians should give adequate information to workers on the importance of a rich protein diet for the various reasons outlined in this communication. Emphasis should be placed upon this again and again in order to have this register adequately in the workers' minds. It might be well to distribute pamphlets containing all of this information with specific directions as to diet fractions, and so forth and how to secure and prepare diets with abundant and palatable protein. As a general rule if the usual protein quantity be doubled in an otherwise apparently healthy individual the diet will be protein rich enough for all practical purposes.

Information should also be distributed by lectures and pamphlets as to the relationship of deficient protein to undue fatigue and to latent or apparent liver parenchymal disease. The workers should be warned and encouraged to report to the company physicians if any of these symptoms appear so that the appropriate tests can be made and measures instituted for the correction of any protein deficiency. Diets should have the guidance of nitrogen balance studies. Under any such conditions, however, a diet as rich in protein as the patient can take, according to the directions herein after given for malnutrition and hepatic disease should be prescribed. Whenever indicated by study of the patient, the diets should be fortified with amino acids and in emergency conditions other methods of administration besides the oral should be freely employed.

In military front-line conditions. Soldiers have always been provided with portable and emergency extra rations in which carbohydrate was the main ingredient on the theory that carbohydrate was what the soldier needed most, and because of its quick utilization and effect. It appears from the newer knowledge that while carbohydrate is truly valuable, protein is much more valuable because of its increased and more prolonged effect and from the standpoint of guarding the individual against infection in wounds, increasing his healing abilities, giving a greater sense of well being and preventing or neutralizing fatigue.

Under such conditions it seems better to enrich the protein content of these rations to at least a 50 per cent increase. Under any battle conditions the protein content of the soldier's diet should be the richest which can be provided.

Methods and rules of administering protein therapy in pathological states in practice

1 Increase the dietary protein intake to between 150 and 180 gm per day. Usually the patient will not or cannot take more by mouth.

2 Use gastric intubation if possible. This may add as much as 50 per cent to the dietary intake. However if too much is given, the subjects become distended develop diarrhea, and much protein is lost.

If because of a digestive or other disability the amount of protein taken is not sufficient, the discrepancy should be made good by adding a sufficient quantity of amino acids dissolved or mixed with the food. This is easily done in feeding by mouth and even more easily accomplished by intubation.

3 Give protein by the intravenous route.

a Transudate (pleural or ascitic) fluid. The protein concentration will vary between 2 and 4 per cent. Usually great bulk must be given to make up for the lack of concentration. It is, perhaps, best to give a moderate quantity at the first administration (250 cc.) as a test for any possible untoward reaction. If any reaction takes place, it might be advisable to use fluid from another donor source. Thereafter if enough transudate fluid is available, one can give as much as 500 cc. every other day in moderately severe deficiency conditions, and in exceptional cases this amount may be given every day. More than the usual care is necessary to ensure sterility otherwise reactions are more common than in other transfusions especially if any source of infection is present.

A coagulum frequently forms in the pleural transudate. This should be filtered out through eight or ten thicknesses of gauze, and at the same time the fluid will be cleared of any cellular content. The protein lost in the coagulum is very small—frequently only $\frac{1}{4}$ per cent or less, of the total contained in the transudate. The transudate fluid should be kept warm (not over 56 degrees) during the transfusion.

The use of transudate fluid will find its best place in the replacement therapy of nutritional edema.

Transudate fluid should be an important source of protein for replacement in chronic protein deficiencies. Possibly when it is furnished commercially methods of collection, processing and preparation will be better than those used at

present, and reactions will be eliminated or much lessened.

b. Plasma. One may increase the protein concentration by adding dried plasma from one bottle to freshly dissolved plasma in the usual concentration. As high as a 10-to-12 per cent concentration may be obtained in this way.

Plasma is most valuable in the immediate period after severe and extensive burns. As much as from 4,000 to 5,000 cc. must be given each twenty four hours in order to replace the enormous protein loss through the burned area.

c. Whole blood. This furnishes more protein than transudate fluid or plasma, but the evidence is not sufficient that blood can be used as a source for the protein needs of the organism. 1,000 cc. of whole blood equal 35 gm. of plasma protein and 70 gm. of globin and erythrocyte protein.

d. Amino acids. The solution should be non-toxic, nonantigenic, and biologically adequate. In intravenous use the limiting factor is the amount of vascular sclerosis which might follow. This can be avoided by use of the subcutaneous or intrasternal routes.

A good formula for the parenteral solution is the following

Amino-acids	30 gm.
Solu-B	1 ampoule
Glucose (5 per cent) in normal saline solution	1,000 cc.

A safe rate of speed for the administration is 30 drops to the minute.

Solu B is a vitamin preparation of special potency for intramuscular or intravenous use. Each ampoule contains the following

Thiamine hydrochloride	10 mgm.
Riboflavin	10 mgm.
Pyridoxine hydrochloride	5 mgm.
Calcium pantothenate	50 mgm.
Nicotinamide	250 mgm.

Only one ampoule is given in twenty-four hours.

e. Albumin solution (25 per cent). In chronic hypoproteinemias and protein deficiencies, these suggestions should be followed in the order given in accordance with the needs of the given situation. In cases due to injury (burns, and so on), or in those in which surgery is contemplated or has already been done, it will be found necessary to reverse the order. I. e., begin with parenteral methods and proceed as soon as convenient or practical to a combination of parenteral and enteral methods, and, finally as soon as the patient's digestive powers have returned to the necessary degree, use enteral methods alone.

In chronic hypoproteinemias of long standing, not associated with any form of surgery it is possible, as Elman (6, 7) has done, to evolve a rough equation according to which the protein needs (protein deficit) can be calculated. However this has two disadvantages (1) under the best conditions, the equation is not as accurate as it apparently seems to be, and for safety's sake the calculated amounts should be increased to make up the margin of error; and (2) the underlying disturbance does not respond to correction on any time schedule and continues for an undeterminable period until recovery takes place, therefore it is best not to set any time limit in which the correction is to be made. In some cases, the underlying condition is irreversible and protein replacement therapy must continue indefinitely.

It is better to calculate the daily requirement as follows

$(MED + DL + NUP) \times 2$ in which
 MED = minimum endogenous daily protein need, usually 25 gm.
 DL = daily loss of protein determined from N balance
 NUP = part of diet protein which is not utilized (estimated)

The factor 2 is arbitrarily chosen to make good any error and to furnish the additional protein from which the contemplated gain is to be made in the correction of the protein deficiency. This calculation can be made quite easily and such amounts permit the subject to regain the normal protein content with a speed that the body can tolerate. In good subjects, the arbitrary factor 2 can be raised to 3 and even 4. The presence of any hepatic parenchymal disease of any grade makes for difficulty because of the inherent inability of the diseased liver to metabolize the administered protein. It is important never to overtax the capabilities of the subject to absorb the given amounts as otherwise the endeavor will be fruitless. Ultimately the amount of total protein needed to replace and make good any deficiency is relatively and actually very large.

The observations of Hoffman, Meyer and Kozoll (Preliminary Studies in Amino-Acid Therapy. *Proc. Central Soc. Clin. Res.*, 1944 17. Seventeenth Annual Meeting, Chicago, Illinois, November 3 and 4, 1944) indicate that after the parenteral administration of amino acids the curve indicates that the amino acids leave the blood almost as fast as they enter and since little of the amino acids can be accounted for in the urine, they must have been taken up by the tis-

ses. Retention in the plasma after oral administration is only slightly longer.

Reliance on the plasma protein level as a guide for the efficacy of the administered amino-acid supply is fallacious. Clinical hypoproteinemia represents a far more serious deficiency of tissue protein than that indicated in the plasma protein level. Hypoproteinemia means a loss of tissue protein at least 30 times as great as the plasma protein deficiency. Such deficiencies cannot be alleviated by isolated or haphazard injections of plasma. From Elman's calculation, an average of about 375 gm. of protein is required each day for ten days to raise a serum-protein level from 5 to 7 gm. per cent. Should this regimen give the desired rise in plasma-protein level it does not necessarily mean that an equally successful replacement has taken place in the reserves and tissue proteins. Similar conclusions seem in order for other forms of replacement protein therapy.

In long-standing cases of protein deficiency in which the deficiency is great and the daily nitrogen excretion excessively high, parenteral amino-acid therapy is usually insufficient to remedy the deficiency and plasma and blood transfusion are not feasible because of expense. All parenteral replacement therapy is indicated in acute conditions when the deficiency has occurred suddenly or comparatively quickly. In the long-standing cases most brilliant results appear to be achieved with a long-continued very high protein diet fortified with large oral doses of amino acids, and interspersed, as the need arises, with blood plasma and/or ascitic or pleural fluid transfusions.

The object to be accomplished in chronic protein deficiencies is the building-up of tissue and reserve protein to something like the normal amount. If the available observations are correct it seems that much larger nitrogen balances than those previously thought necessary must be established and retained for a much longer period of time, and the extent of the latter is not predictable but a matter of continued observation. The best guide for the success of the replacement therapy is not the proteinemia level but the gain in total body weight.

THE CLINICAL RESPONSE OF HYPOPROTEINEMIC STATES TO REPLACEMENT THERAPY

The response to replacement therapy of any hypoproteinemia will depend to a large extent upon the mechanism of its production. The severe liver damage of the hepatic type renders hypoproteinemia least responsive to treatment. The posthepatic type of hypoproteinemia associated with burns usually responds rapidly to efficient

early treatment. The response of the hepatic type depends largely upon the length of time the hypoproteinemia has existed and the amount of irreversible damage that has occurred. The prehepatic type responds to treatment in proportion to the nature of the cause.

The favorable effect of efficient treatment in clinical states of hypoproteinemia depends upon (a) the ability to remove the underlying cause (b) the ability to rectify any disturbance of liver function (c) the relative shortness of time for which these two primary factors have existed and (d) the relative lack of pathological anatomical changes such as edema and tissue protein defects. Good and favorable results of efficient treatment cannot be expected when these factors cannot be eliminated or when any degree of infection is present and cannot be controlled.

THE EFFECT OF THERAPY

Adequate knowledge has greatly enlarged the sphere of replacement and enrichment protein therapy as a protective effect (1) for preventing any impairment of the normal functions of the liver (2) for preventing the deposition of fat in the liver cell (3) for a powerful lipotropic activity when abnormal amounts of fat have previously been so deposited, (4) for lessening the susceptibility and increasing the resistance to toxic and chemical injuries, to infection (antibody formation) and to other forms of disease (5) in the treatment of some medical conditions (such as the cirrhoses) in which protein deficiency is both a potential cause of the disease and an important consequence (6) in the treatment of conditions such as burns in which there is a sudden depletion of protein stores (7) in the facilitation of reparative efforts after chemical and/or toxic injury of the liver parenchyma (8) in the better general preparation of patients for any contemplated operation (9) for the prevention of potential specific dangers, such as postoperative hemorrhage (10) in lessening the injurious effect upon the liver cell of drugs of the sulfanilamide group (11) in lessening the risk of general and spinal anesthesia and (12) in enhancing the efficiency of healing in operative and other types of wounds.

Several points have resulted from this study which seem to have a profound clinical importance. In view of the present tendency toward dieting, one should appreciate the fact that this may produce a state of undernutrition protein deficiency and hypoproteinemia, the symptoms of which perhaps little understood until now include (1) loss of weight and strength, (2) loss of stamina or 'pep' (3) various degrees of chronic

fatigue, and (4) a much lessened resistance to disease. In many cases, this latency predisposes to more profound changes, especially in the functions of the liver. And the prevalence of such latent conditions is very little understood at its true clinical importance among the profession.

It seems to be true that fat people are not necessarily "well nourished." In this type of person usually the available protein is relatively overshadowed by the fat content. A surgeon appreciates this because of his experience that such individuals are not good subjects for surgery.

The impression is growing that, clinically, an enriched protein diet is not only advantageous but also very necessary for anyone about to undergo the abnormal physical strain of surgery with its attendant risk of infection, trauma, and so on, and for the prevention of any danger of postoperative hemorrhage. In this regard, the previous belief that a preponderating rich carbohydrate diet was necessary has suffered.

All of these facts have special significance in military and battle conditions and in the convalescing period of any wounded or otherwise injured person. All of these facts have very special importance in industrial practice, as heretofore indicated. In the latter, employers and their medical advisers are only just beginning to appreciate the important relation of an adequately rich protein content of the food of the worker to his productive capacity as the former eliminates fatigue and corrects any latent disease, and thus increases the earnings of the worker and the profit of the employer.

Similarly, it seems that if at any time, there arises the necessity for the administration of any drug which might have a deleterious and/or toxic action upon the liver, one should supply a very rich protein diet, which would have the tendency to forestall such injury.

The relative importance of the protein fractions is only now becoming sufficiently known and understood. The proteins guard the body's ability to replace its losses through ordinary wear and tear as well as through disease and operative procedures, and they increase the readiness of wounds to heal. Dietary protein protects the organism from infection by supplying the material from which antibodies may be fabricated as the consequence of appropriate antigenic stimuli. By virtue of their lipotropic power they help to restrain any tendency to store abnormal amounts of fat in the various organs, notably in the liver. They furnish the factors which control hemorrhage, and an abundant, rich protein supply gives a sense of well-being and vigor and does away with fatigue.

UNKNOWN FACTORS

There seems to be a great necessity for the study of certain hitherto elusive factors which seemingly have a profound effect. Not always do the available methods of therapy and protein replacement bring about the desired results to our clinical satisfaction. For instance, it frequently happens that either plasma or whole-blood transfusions are given and not much change is apparent then a transfusion is given from another donor, and the result seems almost miraculous. It must be, therefore, that certain factors which had not been present previously become available and are provided through the agency of the new donor. Not infrequently these effects are seen clinically.

MEMORANDA ON COMMERCIALLY AVAILABLE PROTEIN HYDROLYSATE PRODUCTS

At this writing only three protein hydrolysate preparations are available on the open market. Each of these is listed below with a short statement as to its method of preparation and its use, as well as with some indications of its advantages and disadvantages.

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Amigen. This product is a pancreatic hydrolysate of casein. Digested close to the limit of pancreatic proteolysis, it is well suited for parenteral use. Limitations to its use are the need for a comparatively slow rate of administration in order to avoid undesirable reactions. The product has high biological adequacy as attested to by many animal experiments. It is available in flasks in dextrose solution ready for parenteral intro-

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Paroxamine Until recently this product was marketed under the name Amino Acids. This hydrolysate is available in bottles containing 100 cc. of a 15 per cent solution of amino-acid materials derived from the acid hydrolysis of casein. The hydrolytic products are fortified by the addition of a reasonable quantity of tryptophane. The biological adequacy of the original product was questioned by Madden and his associates. Since then the manufacturers have devised a new method for the preparation of stable di-tryptophane and this is contained in the new product which is now being distributed for use. The product has been used with success in many clinical conditions. Its parenteral administration must be done cautiously as too rapid a rate will give severe reactions which are attributed to hyperaminoacidemia. This hydrolysate has been recommended also for oral administration but again the question of palatability enters to a very serious extent. Further it is uneconomic to purchase material especially processed to be administered parenterally and then use it orally. This, of course, puts the burden of unnecessary expense upon the patient.

In addition to the foregoing much experimental work is going on with various hydrolysates and other nitrogen-containing preparations. Highly promising results have been obtained by the use of mixtures of crystalline amino acids which seem to be very efficiently utilized and free of many of the adverse effects noted for parenteral hydroly-

sates in the foregoing. The current scarcity of such materials, however, makes it unlikely that they will be in general use for clinical purposes for some time to come.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Muntarhorn S.: Cavernous-Sinus Thrombosis Treated with Heparin and Sulfathiazole. *Lancet*, Lond., 1945, 245, 10.

A case of cavernous-sinus thrombosis or bilateral orbital cellulitis was treated with 42 gm. of sulfathiazole given orally at the rate of 1 gm. every four hours and 1 gm. of soluble sulfapyridine given intramuscularly for three days. Heparin was given in an intravenous glucose-saline drip hourly at first and continuously from the second day onward in all, 120,000 units were given over five days. The clotting time during this period was 16 in thirty minutes. The patient made an uneventful recovery.

ADRIAN VERBURGHEM, M.D.

EYE

Wright, R. E., and Duncan, H. A. G.: The Giant Magnet in Ophthalmic Battle Casualties. *Brit. M. J.*, 1944, 2, 652.

The authors report the case of a land mine casualty from Normandy who was admitted to No. 4 Canadian General Hospital. One of the wounds was a penetrating injury of the left eyeball. A small foreign body was found to be impacted in the retina about 3 disc diameters down and in front of the disc. The entrance wound was minute near the limbus toward 9 o'clock. There was hemorrhage of the retina near the track of the missile but the lens and vitreous were clear. The vision was 20/20. A roentgenograph showed a single minute opacity corresponding in position to the visible foreign body. Operation was performed under novocain infiltration on July 15, 1944, the same day the injury was received. Good rotation was ensured by dividing the mesial rectus. A 3-mm. incision was made in the sclera through a linear diathermy coagulation between points of fine silk suture. The incision was seen to be about 1 mm. from the foreign body which was partially hidden by coagulum. Six short applications of the giant magnet with the tip of a beak shaped terminal on the wound produced no movement. It was considered inadvisable at this time to extract the particle with forceps. The patient was retained for further consideration. The next day the authors were dealing with a minute metallic foreign body in the vitreous of a German prisoner of war by the posterior route and observed a slight rocking of the foreign body at the end of about the tenth short application as the current went off and on. Thereafter the particle made larger excursions from the center of the vitreous toward the wound and was delivered through the choroid (which had not been

incised) at the thirty-fifth application. The immediate postoperative progress in this case was uneventful; the eye remained quiet, the vitreous clear and the vision 6/6. This experience encouraged the authors to continue with the magnet extraction in the case tried the day before. On July 28 the sclera was exposed down to the previous wound and the curved terminal placed against it toward the side away from the foreign body. The magnet was then used in short bursts of about four seconds (on a few occasions as long as fifteen seconds) for 75 applications. The current was flowing probably for not more than a total of ten minutes. During this time the foreign body was observed to rock in its bed of coagulum, gradually come out of it and lie across the wound. The magnet was then too hot to manipulate and it was considered that its insulation was in danger. The patient was returned to bed. On August 2, under continuous pentothal anesthesia, the mesial sclera was freely exposed and the internal rectus was divided again to give free access. The sclera suture was removed from the original wound on which the beak-shaped terminal was placed. The wound elevated slightly at the first magnet application and the particle, smaller in size than the head of a 35 inch pin came out at the sixth trial without any hemorrhage or discharge of vitreous. The post-operative course was uneventful, the vitreous remained clear and vision was good (6/6 with lens).

It has long been known that intermittent applications repeated at a number of sittings will succeed in moving a feebly magnetic particle. It may not be generally realized that a small magnetic foreign body or larger feebly magnetic particle may behave as a nonmetallic foreign body for a considerable number of magnet applications and be labelled as such. Moreover with such particles the magnet test of pain production in a cocaineized eye is useless.

There are further lessons to be learned from this case and other recent cases observed:

1. The posterior route is ordinarily best for the removal of foreign bodies in the posterior segment.

2. The shortest route to the exterior is probably always best provided it does not drag the particle over or through an intraocular part or structure of relatively greater importance than that in which it is lodged.

3. A beak-shaped magnet terminal is almost essential for work well behind the equator; a blunt core shaped terminal is sometimes dangerous, especially with highly magnetic large bodies, unless they are situated in the anterior segment since the field is too diffuse to direct the delivery accurately.

4. It is possible that the removal of small metallic intraocular foreign bodies of feeble magnetism (as

in the case of iron compounds) is determined by the patience and perseverance of the operator and the patient, and the life of the magnet and rectifier more often than we have thought heretofore.

5. It is perhaps stating the obvious to say that examination of intraocular foreign bodies lodged superficially in the skin of the face or body or in the conjunctiva, is desirable in order to determine their composition and magnetism.

6. To those accustomed to the localization of foreign bodies in civil hospitals in peacetime the slower and less accurate methods necessitated by war conditions constitute a great handicap.

7. The fact that frequent applications of the giant magnet increase the magnetism of feebly magnetic alloys should influence the technique.

8. The application of a surface diathermy terminal to the sclera in the neighborhood of a metallic intraocular foreign body is likely to produce an uncontrollable reaction emanating from the foreign body. For this reason and because of the greater difficulty of withdrawing a magnetic particle from a bed of coagulum, it is probably better technique to apply diathermy to the neighborhood of the scleral wound after the foreign body is removed.

9. If prolonged applications of the Army portable giant magnet are required as in the case described it is almost essential to place it on an adjustable stand with a tilting top beside the operating table.

CHARLES BARON M.D.

Dunnington J. H., and Sellmann, L. von: Penicillin Therapy in Ophthalmology. *Arch. Ophth.* Chic., 1944, 33: 353

Ten clinical cases of eye conditions treated with penicillin are reported, and the difficulty in evaluating the role of penicillin in determining their subsequent course is discussed. The effectiveness of treatment in infections of the lid border and conjunctiva with pyogenic cocci and gonococci seems well established. There are as yet too few cases to permit an adequate opinion regarding many of the deeper infections of the globe. Some of the clinical cases were given simultaneous sulfonamide therapy and the combination may prove to be more effective.

Experimental work was carried out on rabbits whose lenses were inoculated with the staphylococcus aureus. Iontophoretic application of penicillin, after an interval of six hours, checked the infection in none of the cases. When penicillin was injected into the lens six hours after inoculation the infection was checked in all of the cases but when twenty-four hours elapsed it was checked in only 2 of 10 cases.

Further experimental work was done by the direct injection of penicillin into the vitreous. Staphylococcus infection in the vitreous was arrested with a single injection of penicillin when administered within twelve hours after inoculation. If a period of twenty-four hours elapsed between the inoculation and the treatment the infection was not successful.

The injection of penicillin into the anterior chamber of the rabbit caused only a transient inflamma-

tory reaction of mild degree lasting from one to three days, and the authors conclude that this may be an effective method of administering penicillin in the human eye when transcorneal introduction by iontophoresis cannot be used.

WILLIAM A. MAMON M.D.

EAR

Patterson, W. H., and Smith, G. S.: Latent Mastoiditis in Infancy. *Brit. M. J.*, 1944, 2: 659.

In a series of 120 autopsies in infants and young children, pus was found in the mastoid cavities of 71. Although the highest incidence was observed among patients with a clinical history of diarrhea and vomiting, pus was found almost as often in patients with a wide variety of conditions. Clinical postmortem, and bacteriological findings suggest that so-called "latent mastoiditis" is not an etiological factor in the diarrhea-and-vomiting syndrome.

CHARLES BARON, M.D.

NOSE AND SINUSES

Whalen E. J.: Sulfonamide Compounds in the Treatment of Infections of the Nasal Sinuses. *Arch. Otol. Chic.*, 1944, 40: 481

The sulfonamide compounds Whalen declares, are not effective as bacteriostatic agents when used on the unbroken surface of the skin or of the mucous membrane. It is for this reason that it seems illogical to use solutions or suspensions of these drugs for local application to the unbroken mucous membrane of the nose with the expectation that disease-producing organisms in the soft tissues will be affected or controlled. The oral or the intravenous administration of these new chemical agents is the only means by which they can be brought in contact with the disease-producing organisms that are lodged in the lining membranes of the nasal sinuses. They must be used early in the acute infection before the infected area is closed off by thrombosed vessels.

Rhinologists must review their pathology, revise their surgery and integrate their knowledge of the new chemotherapeutic agents. With proper timing of indicated surgical intervention, co-ordinated with systemic use of the new drugs and the application of selected bacteriostatic substances to the field of surgical operation sinus infections of many types can be brought quickly under control.

The local use of sulfadiazine in the concentration of 2.5 per cent in aerosol was found to be without effect in controlling the progress of nasal sinus disease either the acute or the chronic type. Wetting agents were used as vehicles to carry the sulfonamide compounds in the belief that their detergent characteristics would aid in the penetration of the ostium of the sinuses. The experiment was a complete failure. An attempt at forcing the sulfonamide compounds into these cavities by the displacement method of creating a partial vacuum in the sinuses was without success since contrast mediums and other

solutions were found only in small quantities and in a limited number of the sinuses so treated.

The only successful mode of chemotherapy for disease of the nasal sinuses was found to be that of giving full doses of the sulfonamide compounds by mouth. This treatment must be carried on under observation in a hospital where bacteriological studies can be made, the blood level controlled, and the blood picture and renal functions frequently observed. With this treatment a large number of sinus infections both of an acute and a chronic nature can be brought under control.

NOAH D. FAIRCLOTT, M.D.

NECK

Figt. F. A., Rowland, W. D., and New, G. B.: Cyst adenoma of the Larynx; Report of 4 Cases. *Arch. Otolar. Chic.*, 944, 40-445.

A cystadenoma may be defined as an adenoma that has undergone cystic degeneration. Adenomas and cystadenomas may originate in any part of the larynx, except possibly the free edges of the vocal cords since these are covered with squamous epithelium and are practically devoid of mucous glands. The most frequent sites of origin are the ventricles, ventricular bands, epiglottis, and subglottic region. The tumor may range from a few millimeters to several centimeters in diameter. The cystic character of the growth may or may not be evident on clinical examination. A single large cyst may be present or

the tumor may be multilocular. Commonly the growth is covered with normal appearing mucous membrane, but in some cases the mucous membrane is thickened and injected. The enlargement may be slightly yellowish in areas or throughout its extent because of the fact that the cystic contents show through.

The treatment of these tumors depends on their situation and size. Readily accessible lesions of limited extent can be removed by indirect or direct laryngoscopy but extensive growths may require laryngotomy. Indirect removal using a curved forceps and electrocoagulation is feasible but is gradually becoming a lost art in the treatment of benign laryngeal neoplasms generally. Direct laryngoscopy using either the laryngoscope or the suspension apparatus, is preferable in most instances. Suspension laryngoscopy usually is the treatment of choice for the removal of these tumors since it affords a wider field of vision than other methods and permits the surgeon to use both hands, which enables him to carry out limited dissection. If the tumor extends deeply in the region of the ventricle or into the ventricular band, or if it is growing beyond the larynx, thyrotomy probably will be necessary.

Unless the tumor is obviously benign and well localized and its limits are definitely evident on direct examination biopsy should be performed before treatment is instituted. The picture presented by a cystadenoma of the larynx may be closely simulated by a malignant tumor developing in the ventricle.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS CRANIAL NERVES

German, W J Brody B. S. and Harvey S. C.
Compound Craniofacial Injuries. *Surgery*
1944, 16: 374.

A review of the treatment of compound craniofacial injuries is made and a comparison of earlier methods of treatment and results with those of the present day is made. A series of 64 cases of compound craniofacial injuries was treated at the New Haven Hospital, New Haven, Connecticut. The early treatment of such wounds is emphasized as important in avoiding infection and the complications which result therefrom.

The general policy of treatment as outlined included (1) immediate treatment of shock, if present (2) inspection, not palpation of the wound (3) roentgenography to determine the extent of fracture especially the depression or the sinus involvement and (4) operation within six hours in all patients surviving the preparatory period. Local anesthesia was the anesthetic of choice.

The surgical procedure followed in this series, and recommended by the authors, included (1) thorough debridement of the scalp cranial wound and devitalized brain tissue (2) removal of undriven bone fragments and foreign bodies (3) closure of the dura with silk, if possible (4) closure of the scalp in two layers with silk and (5) drainage of the frontal sinus, and of most wounds, for culture. The bone removal was usually en bloc for the comminuted and depressed fractures unless the frontal or sagittal sinuses were found to be involved in which case fragments were removed.

The mortality rate in this series showed a marked increase with the advancing age of the patients. All patients in the seventh and eighth decades succumbed.

Of 51 patients who lived more than six days 20 per cent had postoperative infection. The total mortality in the series of 64 patients was 26.5 per cent.

HOWARD A. BROWN M.D.

Lanigan J P: Traumatic Subdural Effusion in Children. *Lancet, Lond.* 1944, 2: 686.

Three cases of subdural effusion in children are reported. The patients gave a history of trauma which had been followed by signs of increased intracranial pressure and a localizing condition indicative of a gross lesion. At operation a quantity of clear fluid was encountered beneath the dura, and upon release the brain resumed pulsation and gradually began to come up to the dural level. Improvement was very prompt from the standpoint of consciousness and decrease in the motor disturbances.

Operation consisted of exposure through a trephine opening, which was slightly enlarged for purposes of vision.

HOWARD A. BROWN M.D.

Meacham, W F Smith, E., and Pilcher C.:
Chemotherapy of Intracranial Infections; The
Treatment of Staphylococcal and Pneumococ-
cal Meningitis with Sulfathiazole and Sulfadiazine. *W or Med.*, Chic., 1944, 6: 378.

The authors have undertaken a series of studies on cranial infections, and the present article the fifth in the series, concerns the treatment of staphylococcal and pneumococcal meningitis with sulfathiazole and sulfadiazine. The report deals with the results obtained in 116 experiments in which the same types of meningitis were treated by oral administration of sulfathiazole and sulfadiazine, and in 36 experiments in which the intrathecal administration of a suspension of microcrystalline sulfadiazine was employed. Experiments were carried out in groups of 12, half of each group being treated and the other half being kept as untreated controls. The treatment was begun forty-eight hours prior to the external injection of the organisms. The treated animals were given 0.5 gm. of the drug orally every eight hours.

In the first experiments, the staphylococcal meningitis was treated by oral administration of sulfathiazole and there was no significant difference between the treated animals and the controls.

In the next group the meningitis was treated by the oral administration of sulfadiazine, and in this group the mortality was definitely lower. Three groups of 12 dogs were treated by the intracranial injection of a suspension of microcrystalline sulfadiazine. Following this, no convulsions were seen, but several animals had an extreme transitory opisthotonos immediately following the injection, and at necropsy a thick, pasty layer of the drug was found to extend far forward under the base of the brain.

With regard to pneumococcal meningitis, this was produced in 4 groups of 12 dogs and these were treated with sulfadiazine and sulfathiazole by mouth. Higher concentrations of sulfadiazine were found in the spinal fluid of these dogs than in those suffering from staphylococcal meningitis. In fact, the percentage of recovery from pneumococcal meningitis was proportional to the concentration of sulfadiazine in the cerebrospinal fluid.

From these studies it is apparent that, in conformance with previous observations, sulfadiazine was present in much higher concentration in the spinal fluid than sulfathiazole after oral administration. The staphylococcal meningitis produced in these experiments was not benefited by the oral use of sulfathiazole. On the other hand the oral administration of sulfadiazine was distinctly beneficial. Intrathecal injections of microcrystalline sulfadiazine were not considered beneficial in fact, they were believed to be harmful. A high concentration of sulfadiazine in the spinal fluid is essential for recovery from experimental pneumococcal meningitis.

ADRIAN VERBURGEN M.D.

Collis, J. L.: The Etiology of Cerebral Abscess as a Complication of Thoracic Disease. *J. Thorac. Surg.* 1944, 13: 445.

The incidence of brain abscesses following infection in the chest cavity and the route followed by the infection from the thorax to the brain have been somewhat prematurely taken for granted. This study was made for the purpose of clarifying views on these matters. Forty-six cases were collected from the Brompton Hospital, from the Birmingham United Hospital, and from an E. M. S. Chest Center in England, and the first 44 of these were used for compilation of statistical tables.

On reviewing the various tables submitted with regard to certain general factors involved in this type of brain abscess, some of these factors were regarded as of negative value for instance, the age, the side, and the site of the abscesses, the infecting organism, the number of abscesses found, and the side of the primary condition of the chest were so varied as to indicate nothing in particular. A second group of factors, however, were regarded as significant namely the preponderance of these abscesses in the male sex, the special clinical picture of this type of brain abscess, the similarity of the various aspects of the brain abscess—whether they were secondary to lung abscesses, empyema or bronchiectasis, the fact that the brain complications might follow disease in the lung or in the pleura, the fact that only chronic disease of the chest caused brain abscesses, the increased danger of this complication following surgical interference, and the absence of abscesses in other parts of the body associated with involvement of the brain.

The author was particularly interested in the manner in which the infection spread from the lung or pleura to the brain. It was first suggested that the connection was due to the passage of septic emboli from the lung to the brain. Although this has been a popular theory it has never withstood anatomical or experimental criticism. Although it might be true for the pulmonary circulation it certainly is not true for the pleural circulation which is involved in cases of empyema. Furthermore, very little cerebral manifestation of septic emboli has been observed clinically in the patient, and the classical picture of cerebral embolus has certainly not been fulfilled.

With the rejection of this theory the theory of parasagittal infection developed but there were many objections to it, particularly in cases of empyema, which are almost cured at the time that the brain abscess develops and the patient cannot at that time be said to be in a chronic septic state. The spirochetal theory was also examined, but as far as the author is concerned, he was not able to demonstrate spirochetes in the brain of any of his patients in the region of the abscess, but there are many artefacts which will give this false impression. Congenital heart disease such as patent foramen ovale was also investigated, but was not properly connected with this group of cases. It is apparent throughout that the place of empyema in the formation of brain abscess

is the stumbling block because the pleura has a different circulation from that of the lung.

In order to obtain information concerning other conditions in which substances pass from the lung to the brain, carcinoma was investigated. Whereas bronchial carcinoma most commonly causes metastases to the brain, carcinoma of the breast is in second place and the latter of course is a chest wall condition. It appears then that the only vessels which communicate between the lung, the chest wall, and the brain are the bronchial and intercostal veins, which drain into the azygos veins, the spinal veins also drain into the azygos system. These veins are valveless and gravity plays an important part in their flow.

Experiments were continued in which opaque materials were injected into intercostal veins, and it was surprising to find the ease with which the opaque material reached the brain via the inside of the spinal canal. It was attempted to reproduce the disease in cats, but, unfortunately this was unsuccessful. Experiments of this nature will have to wait until monkeys are available.

In view of this discussion and experimental work, considerable evidence was produced in favor of the fact that infected material is carried from the chest to the brain via the spinal veins.

ADRIAN V. LUBCHENCO, M.D.

Harris, W.: Paroxysmal and Postural Headaches from Intraventricular Cysts and Tumors. *Lancet*, Lond., 1944, 247: 654.

The author points out that cysts of the third and lateral ventricles often produce no physical sign, but may present the so-called classical triad of periodic headaches, vomiting and papilloedema. Such a syndrome would lead one to suspect the possibility of periodic obstruction of the ventricular system. Three cases of this type have been reported.

HOWARD A. BROWN, M.D.

Hammes, E. M., Jr.: The Reaction of the Meninges to Blood. *A. A. New Psychiat.* Chic., 1944, 311: 505.

Autogenous blood in the subarachnoid space of human patients is not well tolerated by the leptomeninges.

The meningeal reaction to blood is evident within two hours of the hemorrhage and begins as an outpouring of polymorphonuclear leucocytes, followed by the appearance of lymphocytes and large mononuclear phagocytes derived from the mesothelial lining cells of the arachnoid.

This cellular reaction is transient and persists only as long as blood, or products of breakdown of blood, are demonstrable in the subarachnoid space.

Permanent effects occur in the form of patchy fibrosis of the pia-arachnoid, with obliteration of the subarachnoid space. This can be demonstrated only after the blood has been present ten days or longer.

From this study, no conclusion can be drawn as to the effect on this meningeal reaction of drainage

d bloody cerebrospinal fluid by repeated lumbar puncture.

Rupture of an intracranial aneurysm is capable of producing sudden death. The patients rarely if ever have an associated intracerebral hemorrhage although intracerebral bleeding is a very common finding among those who survive the immediate result only to succumb hours or days later.

Intraventricular hemorrhage sufficient to produce dotted blood in the ventricles will not occur following rupture of an intracranial aneurysm unless there is an associated intracerebral hemorrhage.

SYMPATHETIC NERVES

Smithwick, R. H.: The Surgical Treatment of Hypertension. *N. York State J. M.*, 1944, 44: 3093.

The author discusses some of the problems of choosing the proper cases for lumbodorsal splanchnicectomy. A review of the clinical investigations during the past eleven years is used as a basis for the choice of patients who may be suitable or unsuitable for surgical treatment of this type. The details of the operative procedure have been described elsewhere.

In nearly all of a series of 156 cases, there was a significant and persistent lowering of the diastolic blood pressure following operation. This was associated with favorable changes in the eyegrounds, electrocardiograms, and in cardiac and renal function.

The results have been variously divided into groups, according to the degree of drop in the diastolic pressure. The results in women have been significantly better than in men. The cases have been divided into three types, according to the degree of pulse pressure. Surgical results have been poorest in patients with the highest pulse pressure.

The report is based on 215 patients of whom 179 are living from one to five years following operation, and of whom all had had diastolic blood-pressure levels between 100 and 170 prior to operation. All patients had been subjected to a detailed study from the standpoint of their cardiac function, renal function, and vascular status as estimated by examination of the fundi. They had also been subjected to postural and cold blood-pressure tests. Their blood-pressure response to sedation should be studied.

The decision as to operative advisability was based upon the evaluation of all these studies. Certain contraindications to surgery have been outlined. (1) patients with congestive heart failure and impaired kidney function, with elevated nonprotein nitrogen, or a reduction in intravenous phenolsulfonphthalein (an output to below 15 per cent in the first fifteen minutes) (2) male patients with resting diastolic levels of 140 or more unless they have had a cerebral vascular accident and there is no evidence of actual impending cardiac failure or failure of kidney function (3) women patients with resting diastolic levels of over 140—the same rule applying

as to men except that in the male it is suggested that the phenolsulfonphthalein output must be 20 per cent or more during the first fifteen minutes, while in women, operation may be contemplated if the phenolsulfonphthalein output is as low as 10 per cent or more during the first fifteen minutes.

Other tentative suggestions are made with regard to patients in certain special groups in which a study of the surgical results has indicated a probably poor result.

HOWARD A. BROWN, M.D.

MISCELLANEOUS

Peterson, E. W. Kent, B. S. and Cons W. V.: Intracranial Pressure in the Human Subject at Altitude. *Arch. New Psychol.* Chic., 1944 52: 520.

The authors undertook to study the effects of altitude on the human intracranial pressure in a patient with a large cranial defect. The cranial defect measured 16 by 10 by 2.5 cm. and was perfectly healed and freely mobile under stresses of artificially increased pressure.

The degree of herniation of this defect was measured when the patient while breathing oxygen was taken to an altitude of 30,000 feet at the rate of 3,000 feet per minute in a decompression chamber. Readings were taken every 10,000 feet on a specially improvised apparatus. Readings were taken also at 25,000 feet after the subject's mask had been removed for two minutes and twenty seconds. There were no significant changes in the intracranial pressure either while the subject was breathing oxygen at an increased altitude or while he was in an acutely anoxic state (exposure of two minutes and twenty seconds at an altitude of 25,000 feet).

With a specially constructed plethysmograph carefully fitted to the cranial defect further observations on the intracranial pressure failed to reveal significant alterations when the subject was breathing oxygen at altitudes of as high as 25,000 feet and when acute anoxia of from sixty to seventy seconds duration was induced at this altitude. With the same plethysmograph technique of recording changes in intracranial pressure, again no significant alterations were recorded either on ascent or descent when the patient was taken to 15,000 feet and kept at this level without oxygen for twenty minutes. A further ascent to 20,000 feet, where the patient remained for ten minutes without oxygen, likewise failed to cause a significant change in the intracranial pressure as recorded on the plethysmograph.

Direct observations were made on the intracranial pressure by means of lumbar puncture. In intact skull was simulated in this patient by closing the cranial defect with a plaster cast. In ascent to 30,000 feet with the patient breathing oxygen did not cause any increase in the spinal fluid pressure. As has been observed by others, minute bubbles were noted to be rising in the manometer after an altitude of 20,000 feet had been reached. Removal of the oxygen mask for ten minutes at 20,000 feet caused an increase of

only 23 mm. of spinal-fluid pressure. This was noted toward the end of the exposure to anoxia and the administration of oxygen caused no change in this pressure.

It was concluded that all of these approaches to the determination of the intracranial pressure showed that no significant increase in the intracranial pressure of man occurred at high altitude and under conditions either of sudden or of more prolonged anoxia. This is contrary to the conclusions of other workers in the field and is of importance insofar as it indicates that head injury casualties may be safely evacuated by air. **HENRY A. SUMNER, M.D.**

Peterson, E. W. Bornstein M. B., and Jaepser H. H. L.: Cerebrospinal Fluid Pressure under Conditions Existing at High Altitudes: A Critical Review. *Arch. New. Psychiat., Chic.*, 944, 5 400.

This is a critical review of the literature based on available reports relating to this subject. High altitudes result in the following changes: reduced barometric pressure, reduced temperature, and reduced tension of oxygen. There is no change in the percentage composition of the atmospheric gases.

From their review the authors conclude that reduced atmospheric pressure has very little influence on the intracranial pressure itself, however expansion of gas in the bowel at reduced pressure may increase the intracranial pressure secondarily to a rise in venous pressure. Cerebral edema may occur and cause increased intracranial pressure because of anoxia. It has been found that the arterial blood increases because of the anoxia of high altitude and this may be a further factor in increased intracranial pressure in the initial stages. It has been believed that the increase in intracranial pressure as analyzed by experts in the field, was not of sufficient magnitude to be of clinical significance.

The conclusion reached in this highly critical study is that significant increase of intracranial pressure will not occur in the sick or wounded during transportation by air provided anoxia is not permitted to occur. **ANDREW VANDERBOOMER, M.D.**

Peacher W. G., and Robertson, R. C. L.: Neurological Complications Following the Use of Continuous Caudal Anesthesia. *Arch. New. Psychiat., Chic.*, 944, 52 531.

Two cases of infection complicating the use of continuous caudal analgesia, which resulted in neurological changes, are reported.

The first case was one of immediate bilateral sciatica following forty-eight hours of continuous caudal analgesia. Objectively there was a sacral anesthesia with hyposthesia as high as the second

lumbar segment on the right, and as high as the fourth lumbar segment on the left. The cause of this proved to be a localized infection in or about the caudal subarachnoid sac. Culture of fluid aspirated from the caudal canal yielded the hemolytic streptococcus and the staphylococcus albus. Frank pus was obtained on lumbar puncture through the fourth lumbar interspace, a culture of which gave pure staphylococcus albus hemolyticus. No spinal fluid was obtained with this procedure and it could not be determined whether the pus was intra or extradural. Sulfathiazole (6 gm. daily for two weeks) was given, and the patient improved rapidly. She was asymptomatic and neurologically negative on discharge twenty four days postpartum and also on follow-up examination made one and one half years later.

The second patient had a normal delivery with sixteen and one-half hours of continuous caudal analgesia. Her postpartum course was normal until the ninth day after delivery when she complained of low back pain with bilateral sciatic radiation. There was questionable sensory impairment below the third lumbar segment, and bilateral Kernig and Brudzinski signs were present. There was a daily temperature elevation of 103 degrees. Remission occurred with the use of sulfadiazine, but six weeks postpartum the patient was readmitted to the hospital with a recurrence of symptoms. At this time there were hyperactive reflexes and bilateral Babinski signs, as well as signs of meningeal irritation. The temperature was elevated daily to from 100 to 101 F, and there was a leucocytosis of 14,800. Multiple lumbar punctures indicated the presence of a partial subarachnoid block between the second and the fifth lumbar interspaces, and pantopaque myelography gave the picture of a diffuse lumbar arachnoiditis. Laminectomy was performed and the arachnoiditis confirmed the roots of the cauda equina were separated and the dura was left open after a section of tantalum foil had been placed over the roots.

Operation relieved the sensory changes, but sphincter function did not return and lumbosacral pain persisted, as did motor impairment of the lower limbs.

Postoperative x-ray examination revealed an osteomyelitis of the first sacral to the second lumbar vertebral bodies, inclusive. No causative organisms could be identified.

From a review of the literature the authors conclude that the rate of infection in the production of complications following caudal anesthesia is second only to the introduction of the analgesic agent into the subarachnoid space. **HENRY A. SUMNER, M.D.**

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Smithy H. G.: Mixed Malignancy of the Breast. *Surgery* 1944, 16: 854.

The simultaneous occurrence of two different malignant processes at points of origin quite distinct and separate from each other is a well established entity. Much less common than these anatomically unrelated tumors is the presence of two different types of neoplastic tissue growing within the same organ.

Mixed malignancy of the breast can be divided into two categories: (1) the simultaneous presence of two distinct varieties of malignant tumors growing side by side but having no structural intermingling of their elements, and (2) a combination growth of two different malignant tissues, the component parts of which are intimately blended with one another into a single tumor. The first type may be regarded as a coincidental occurrence of two independent neoplasms in the same organ but the second type of mixed tumor of the breast can hardly be considered as an accidental coexistence of different neoplastic lesions. It appears likely that these tumors either arise from a single cell or one element occurs first and subsequently stimulates proliferation of the other.

Experimental observations lend support to the possibility that a malignant lesion of epiblastic origin can stimulate adjacent mesoblastic elements to proliferate, and vice versa. Widely divergent opinions prevail among pathologists concerning the possibility that combination growths can originate from a single cell, and no positive expression can be made at this time.

The authors report in detail an unusual case of mixed sarcoma and adenocarcinoma in a ten year old negro girl. The case is believed to be the first of its kind recorded in a child.

Regarding classification of the tumor it is desirable to avoid such terms as carcinosarcomatodes, carcinosarcoma, and sarcomacarcinoma, which have been employed to indicate the relative time of appearance of the different malignant components of a dual tumor as well as the preponderance of one element over the other. Actually the neoplasm described consisted of two well defined individual malignant tissues. Therefore for the purpose of clarity the authors suggest that it be called a mixed sarcoma and adenocarcinoma. The word mixed is an important qualifying descriptive factor designed to differentiate the tumor from a condition in which the sarcomatous and carcinomatous growths exist as separate, independent neoplasms in the same breast.

The development of a dual mammary neoplasm in a patient at ten years of age is extraordinary. Only 4 authentic cases of carcinoma of the breast have been reported as occurring before puberty.

While removal of the breast was considered necessary it was the impression of several examiners who saw the patient before operation that the lesion was benign, most probably mammary hyperplasia of an extreme degree. Accordingly a simple mastectomy was done. In general, mammary sarcomas rarely invade the axillary lymph nodes so that axillary dissection is generally considered illogical in the operative treatment of this lesion, removal of the breast and pectoral muscles being the procedure of choice. Discovery of the carcinomatous factor was made only after sections of the axillary lymphoid tissue were examined. The involved lymph node was excised only because of its proximity to the incision no attempt being made to dissect the axillary contents. Such being the case, the question arose as to the advisability of a second operation for removal of the pectoral muscles and the lymphoid structures of the axilla and the supraclavicular space, after discovery of the metastatic carcinoma. Probably such a radical procedure should have been carried out, but factors beyond control prevented it.

JOSEPH K. NARAT, M.D.

TRACHEA, LUNGS, AND PLEURA

Bird Acosta, I.: Pulmonary Suppuration Secondary to Cardiospasm. *Am J Roentg* 1944, 53: 481.

Pulmonary suppuration as a result of esophageal overflow has often been reported in the literature. Esophageal retention may be caused by carcinoma of the esophagus, strictures, foreign bodies, pulsation diverticulum, extrinsic esophageal pressure from adjacent tumors, and cardiospasm. Of all the causes of pulmonary suppuration following esophageal overflow cardiospasm, although a fairly common clinical entity is rarely considered.

The author reports 3 cases of pulmonary suppuration as a result of cardiospasm.

MAURICE D. SACHS, M.D.

Davidson L. R.: Hydatid Cysts of the Lung. *J Thorac Surg* 1944, 13: 471.

Hydatid cysts of the lung, while uncommon in this country (36 cases reported in the United States up to 1930) will unfortunately, be much more frequent in the returning soldiers. The geographical distribution of this condition is dependent on its incidence and distribution in reservoir hosts particularly sheep, cattle and pigs and cases are most frequently seen in sheep-raising countries such as Argentina, Uruguay, New Zealand, Australia, Italy, Syria, Greece, and Algiers.

The life cycle of the echinococcus begins in the infected intestine of the definitive host (dog, wolf or jackal) where the taenia are found. The untainted dog is infected by eating the organs of animals (intermediate or reservoir hosts, i.e. sheep or pigs) infected

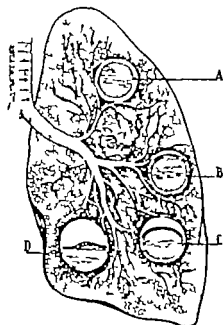


Fig. 1. A, Hydatid cyst of lung; B, perivesicular pneumonia; C, double-domed arch (Cumbo's sign) and D camalote formation (From José Arce).

with fertile hydatid cysts. Man, while also an intermediate host, represents a dead end as far as the further development of the parasite is concerned as his flesh is never eaten.

The taenia echinococcus which resides by the thousands in the intestine of an infected dog is a four-segment tapeworm about 0.5 cm. long. From the terminal proglottid, innumerable ova are discharged which gain entrance into man through contaminated water or vegetables. The egg lodges in the human stomach where the embryo is freed when the coat is digested by the stomach acid. It then migrates through the gastric or duodenal wall, enters the venules, and is carried to the first barrier—the liver. There the embryo enters the larvated stage and, in growing, empties its center and forms a fluid-filled vesicle with an inner or germinal layer and an outer or laminated layer. From the former layer vacuolated masses of cells (brood capsules) protrude into the vesicle's cavity. These in turn give rise to scolices. Most of the capsules and scolices are pinched off the germinal layer and sink in the hydatid fluid to form "hydatid sand." As the vesicle grows it stimulates in the organ the formation of an adventitial layer of connective tissue which is separate from the vesicle but is part of the simple hydatid cyst. If the cyst were in a sheep and the infected organ were eaten by a dog, the ingested scolices would enter the small intestine to become new taenia.

Daughter cysts, usually sterile and without scolices or proliferating vesicles, are generally the result of mechanical, infectious or toxic influence. On

the other hand an infected cyst, if ruptured or aspirated, may discharge scolices into surrounding tissue and cause secondary cysts (secondary hydatidosis). Therefore when operating one must not permit any hydatid fluid or sand to contaminate the incisional or operative wound. For the same reason, one should never aspirate a cyst except at time of operation. If a primary cyst erodes the pulmonary vein, metastatic hydatidosis results.

The simple cyst fluid and membranes are sterile. If they enter a new phase and become complicated infection causes death of the cyst and the contents of the cyst are necrosed and fragmented and the vesicle virtually falls apart.

In the lung the vesicle is surrounded by adventitia and also a concentric layer of atelectasis. If on enlarging the cyst breaks into a bronchiole the perivesicle space communicates with the bronchiole. With coughing and straining, air may surround the vesicle and give a perivesicular pneumonia (B). If a larger opening occurs, air may enter the vesicle and produce Cumbo's sign (C) a double-domed arch. Finally when the membranes sink into the cavity and float upon the remaining fluid the camalote (D) formation is noted. These are considered pathognomonic roentgenographic findings for pulmonary hydatid cysts. (See Figure 1.)

For diagnosis one must recognize the difference between simple and complicated cysts, which may be either peripheral or central. The simple cyst is usually silent. Nonproductive cough is the first symptom. There usually is accompanying chest pain. Later there may be hemoptysis with a productive cough. When the cyst enlarges dyspnea may be manifest. Physical examination often suggests the diagnosis. In case of doubt the place where a patient lives is of utmost importance.

Laboratory methods are of some value in diagnosis but the procedures are not unequivocal. Eosinophilia is not present in dead or suppurating cysts. An eosinophilia (over 4 per cent) may not be present even in living cysts. The complement fixation test (Weinberg) and the more reliable intradermal test of Casanovi are not infallible. Certain diagnosis is made only when hooklets, scolices, or laminated membranes are found in the sputum. Characteristic x ray findings may establish the diagnosis even in complicated cases. Cysts are usually in the lower lobe and occur more frequently in males.

Medical treatment is of no value in echinococcus cysts surgery is the only satisfactory method of treatment. The presence or absence of pleural adhesions determines the type of surgical treatment, the essence of which is opening the chest, incising the cyst, and removing the membranes. The one-stage operation in the absence of adhesions is neither simple nor without definite risk, particularly that of pneumothorax. Central cysts are only attacked when they are draining poorly or when accompanied by fever and then only with caution.

The chest wall is opened over the cyst and the presence or absence of adhesions determined. These

may be shown preoperatively by a pneumothorax, but one may rupture peripheral cysts by pneumothorax. The cyst is entered and the membranes and contents are removed. Adhesions may be formed by packing the wound with gauze and reoperating two weeks later. A one-stage operation for an unadherent lung is accomplished by projecting the lung through the wound in the perietal pleura by using a tight fitting mask and increasing the positive pressure to 10 cm. of water at the appropriate time. The lung, if unadherent, may be sutured to the pleura outside of the cyst area to prevent pneumothorax.

The cyst may be treated in several ways. The wounds are draped meticulously before the cyst is opened. Fluid is withdrawn with an aspirating needle and a 2 per cent formalin is injected. The cyst wall is incised and the membranes are extracted from within the adventitia. The adventitia then may be completely sutured in a simple aseptic cyst, but in most cysts manipulation to establish drainage is the procedure of choice. Fluid is not always obtained in a complicated cyst.

It is not unusual to have a simple cyst leak and rupture into a bronchus or bronchiole. If this progresses, the fluid and the membranes may be extirpated and permit a spontaneous cure. If only the fluid is expelled the membranes remain and one may expect an infection or abscess formation.

The author then reports 4 cases. In the first a simple cyst was removed surgically with complete recovery. In the second case there was an intra thoracic hydatid cyst which may have arisen in the pedicle, body or lamina of the vertebra. The chief complaints were due to cord compression. The patient was operated on twice and is now working as a laborer without a brace. In the third case there was a complicated hydatid cyst of the left upper lobe. This was completely cured by operative drainage. In the last case there was a central hydatid with pneumothorax. Surgical drainage of the chest cavity only was attempted because of the central location. The patient died of a generalized peritonitis six months later without autopsy. ROBERT BICKLOW M.D.

Reinhoff, W. F., Jr.: Present Status of the Surgical Treatment of Primary Carcinoma of the Lung. *J. Am. M. Ass.*, 1944, 126 1123

Reinhoff reports a clinical analysis of and the results in 181 consecutive cases of primary carcinoma of the lung in which operation was performed over an eleven year period. Of this group 71 or 39 per cent, were operable. The sex incidence was 6 to 1 in favor of males the incidence of involvement of right and left sides was approximately the same. Sixty four of the patients were in the fourth to sixth decades, inclusive. The signs and symptoms that predominated in the order of their frequency were cough, hemoptysis, pain, weight loss, hyperpnea, pneumonitis, and fever. In general, there are no characteristic signs and symptoms of this disease—the lesion masquerades as many of the commoner disorders of the lung.

In this series of 181 cases the roentgenogram of the chest was positive in every instance. This diagnostic measure is the most important and the simplest method of examination. Second to x ray study is bronchoscopy.

In 70 per cent of the cases subjected to pneumonectomy there were metastases to the bronchial and tracheal nodes.

The microscopic appearance of these lung tumors made it possible to divide them into two large groups (1) the flat and (2) the squamous-cell carcinomas. The former gave a better prognosis.

The surgical treatment consists of total pneumonectomy. In this series 95 total pneumonectomies were performed the immediate mortality being 25 per cent. Thirty five per cent of the patients surviving are alive and well from one month to eleven years after the operation.

An otherwise fatal disease, primary carcinoma of the lung can be satisfactorily treated by surgical removal of the entire organ. Surgical measures short of total pneumonectomy are not efficacious. Post operative mortality and longevity are at least as good as, if not better than the postoperative results following the surgical treatment of carcinoma of other organs. J. M. MORA, M.D.

Kent, E. M., and Sager, W. W.: Current Practice in the Treatment of Thoracic Empyema. *Surg. Clin. N. America*, 1944, 24 1492.

The authors described their management of thoracic empyema at the United States Naval Hospital, Bethesda, Maryland. The choice between open and closed drainage is discussed. Open drainage is preferred when localization has occurred and when the pus is thick, such as in pneumococcal infections. When the pus is thinner especially with organisms such as the streptococcus or staphylococcus and when the empyema space is a large one they prefer closed drainage. By closed drainage is meant the insertion of an intercostal tube or catheter the distal end of which is placed under water. Later on it may be necessary to resect a rib and drain the cavity by open drainage. Tidal drainage may be used especially with the closed type of drainage when pus and fibrin obstruct the catheter.

It is estimated that 80 per cent of pneumonias are caused by the pneumococcus and the remainder by a variety of organisms. This holds true for empyema also but there is some variation from year to year and from place to place. Before the use of sulfonamides in the treatment of pneumonia the incidence of complicating empyema was from 5 to 6 per cent, but since the use of the sulfa drugs the incidence of complicating empyema is from 1 to 2 per cent. This decrease in the occurrence of empyema is found chiefly in the pneumococcal infections.

The fundamental principles are the same in both types of drainage. It must be carried out in a dependent position and maintained by close management. The tube must not become obstructed by fibrin or granulations; it should be shortened as the

cavity becomes obliterated rather than by a routine method for all cases. If the tube should slip out it must be replaced soon, because the opening in the chest wall contracts within a few hours and it may be impossible to reinsert another. The size of the cavity may be determined by filling it with sterile solution at intervals, or by x ray examinations. The tube should be left in place until the space holds less than 10 cc.

When an empyema has formed under sulfa treatment for the primary lung infection it is often atypical. It may be loculated, nondependent, or interlobar and often requires more than one drainage. However the use of the drug decreases the incidence of empyema, and if thin fluid forms it may be sterilized without the formation of thick pus. The local use of the sulfa drugs is of questionable value.

Next to the pneumonia as the primary cause of the pleural infection is the intra abdominal suppuration with subdiaphragmatic abscess and, later on supradiaphragmatic extension. The organism here is often the colon bacillus.

The treatment of empyema with penicillin is not yet entirely standardized but the experience to date is sufficient to lead to certain conclusions which however may need to be revised at a later date. The best chances of success are in the early thin effusions before frank pus is formed. Of course, the type of organism and its vulnerability to penicillin are the main factors which will determine its successful use. Both parenteral and local use should be resorted to as parenteral use alone does not give high enough concentrations in the pleural cavity. Five hundred units per cubic centimeter is the concentration for local instillation. The pus should first be aspirated and one half that volume of penicillin used for replacement.

Once frank pus is formed, drainage is usually required as thick pus and fibrin masses cannot be aspirated. Even though the cavity may be sterilized there remains the thickened pleura and fibrosis which lead to chronic empyema. Cases of penicillin failures are illustrated.

The development of bronchopleural fistula as a complication of empyema is a serious one and may lead to months of convalescence. When the x ray film demonstrates a fluid level and when air has not been allowed to enter the pleural cavity a fistula must be assumed to be present. Early recognition is important, as closed drainage will often cause a spontaneous closure of the fistula. In cases in which the fistula does not close the morbidity is high and chronic empyema usually results. For such cases Blades is quoted as using a decortication operation through an intercostal incision, and the incision is closed tightly with closed catheter drainage and suction. The released lung may be readily expanded and caused to adhere to the parietal pleura. Should the fistula reopen it is of relative unimportance as the lung has adhered to the thoracic wall.

FORESTER D. DOORLEY, M.D.

HEART AND PERICARDIUM

Niklin, D. C.: Wounds of the Heart. *Ann. Surg.*, 1944, 120: 87

This report concerns the operative treatment of 23 cases of wounds of the heart, or intrapericardial portions of the great vessels. There were 5 deaths in this series, a mortality of 22 per cent, as compared with a 42 per cent mortality in a previously reported series of 38 similar cases. In the present series there were no deaths from infection. Those patients who did not recover either died on the operating table, or shortly after operation, presumably from hemorrhage or the effects of tamponade. The reduction in mortality from infection was not due to the use of sulfa drugs, since they were used in only 1 case for the treatment of postoperative pneumonia. In no instance was a sulfa drug placed in the wound. The reduction in infections is believed to be the result of more careful preoperative preparation and a more meticulous technique. Another possible factor is the lowered mortality has been the giving of intravenous fluids to the last 8 patients prior to operation. This treatment was based on experimental evidence that rapid intravenous infusion with subsequent increase in the blood volume, enables a dog to withstand a considerably higher intrapericardial pressure. In each patient receiving intravenous infusions there was clinical improvement preoperatively.

The indication for operation in all cases was the finding of definite evidence of cardiac tamponade. This diagnosis was based on lowered arterial and increased venous pressure, and the presence of a quiet heart on fluoroscopic examination. The latter finding is the most important sign and the one least likely to lead to a mistaken diagnosis. Venous pressure readings are not only of value in the diagnosis of tamponade but are of considerable prognostic importance. If the venous pressure is high, that, in itself, is evidence that the heart is carrying on its functions and that the cardiac output is at least sufficient to produce such pressure. On the other hand, a low or lowered venous pressure in the presence of tamponade is evidence of a failing heart and a greatly reduced cardiac output. In 17 patients arterial pressure was so low that it could not be recorded. In those patients who recovered there was an immediate rise in arterial pressure following the release of the tamponade. Some type of general anesthesia in which positive pressure can be used is preferable to local anesthesia, since the difficulties of heart suture require that the patient be quiet throughout the procedure.

The author has slightly modified his previous opinion that operation should always be performed as soon as the diagnosis of a heart wound is established. Delay is justified if continued improvement follows aspiration without recurrence of signs of cardiac compression, but operation should not be delayed if there is evidence of bleeding into the pleural cavity or through the external opening. In this series, all patients had immediate opera-

tabulated summary of the data on the 23 cases is presented.

JOHN L. LINDQUIST M.D.

Vódice, A.: The Surgical Treatment of Cardiac Syncope, Apparent Death, Cardiac Fibrillation, Stoppage of the Heart (*Tratamiento quirúrgico del síncope cardíaco. Muerte aparente, fibrilación cardíaca, paro cardíaco*). *Rev As méd argent.*, 1944, 53: 937.

During operation with any kind of anesthesia, cardiac syncope may occur. The heart beat stops and there is no arterial circulation. This condition may result from ventricular fibrillation or stoppage of the ventricle. The pressure falls to zero. The patient is apparently dead, although prompt action may restore the heart beat. The brain cannot endure deprivation of the blood supply for more than from two to five minutes and therefore action must be very prompt. Every second counts. Efforts are being made to find some means of preserving cerebral function for a longer time but so far they have not been successful. Experiments in producing artificial fibrillation in animals and then treating it have contributed to the successful treatment of this condition in human beings.

In every operating room the apparatus for treating stoppage of the heart should be at hand. If the heart stops the anesthetist should give artificial respiration to keep up the oxygenation of the lungs, while the surgeon should expose the heart by opening the pericardium and massage the heart with a rhythm of from 50 to 60 movements per minute. After the flabbiness of the heart muscle has been overcome and the beat restored, electrical shock should be given for the purpose of overcoming the fibrillation. The apparatus used for this purpose is illustrated and the technique of the shock described in detail. The shock may be applied 3 or 4 times, or even more if necessary. Patients apparently dead have been restored in this way. Illustrative cases are described.

Supplementary methods are the pouring of 2 cc. of a 5 per cent solution of procaine over the heart before the massage and the injection into the cavity of the right ventricle of 1 cc. of a 1:1000 solution of adrenalin diluted in from 10 to 30 cc. of physiologic salt solution, if massage does not prove effective at first.

AUREY G. MORGAN M.D.

ESOPHAGUS AND MEDIASTINUM

Rankin, L. M.: Perforated Ulcer of Esophagus Following a Burn. *Am. J. Surg.*, 1945, 67: 134.

In 1843 Curling first described duodenal ulcer following a burn. The cause and frequency of this complication are still uncertain. Ulceration of the lower end of the esophagus following a burn is even more rare. A search of the literature revealed only 1 case of perforation of such an esophageal ulcer.

The author presents the case of a four-year-old boy who sustained second-degree burns of both thighs, buttocks, and the lower abdomen. The child progressed very well for four days. He then sud-



Fig. 1. The lower end of esophagus and stomach showing perforation of ulcer of esophagus. (Courtesy of American Journal of Surgery)

denly developed severe pain, following which his condition became worse, and he died within two hours. Autopsy revealed a perforated ulcer of the lower end of the esophagus with hemorrhage (Fig. 1).

No case has been reported in which surgical closure has been attempted, but this gives the only hope for cure.

THOMAS F. THORNTON, JR. M.D.

Hurst, A., and Bassett, S.: Megacosophagus as a Cause of Mediastinal Widening. *Am. J. Roentg.* 1944, 52: 508.

This report deals with 11 cases in which the initial roentgenogram of the chest suggested the presence of a megacosophagus, which was subsequently verified by a barium meal. They were discovered in extensive mass surveys of apparently healthy adults to detect unknown cases of tuberculosis. Nine patients were males, inasmuch as the majority were rejected draftees. One of the most interesting features in the study of megacosophagus is the marked disproportion between the relative paucity of the complaints and the good general condition of the patient on the one hand, and the large size of the esophagus on the other. No benign or malignant



stricture causes dilatation even approaching that produced by "cardiospasm."

Five diagnostic roentgen features were found, as follows:

1. Diffuse widening of the mediastinum. The shape depends largely on the degree and location of the dilatation. The widening of the mediastinum is usually seen beginning at the thoracic inlet or just below. The degree of widening is difficult to measure since the largest dilatation is to the right and the left border is lost in the density of the heart shadow.

2. A definite fluid level was found in 4 of the 11 cases traversing the tracheal column of air at the level of the clavicles. This depends for its presence on recent drinking or eating, but if present is pathognomonic.

3. In the upper esophagus lying to the right of the sternum, there is occasionally seen a peculiar stippled, marbled or mottled density. This is due to the contrast created by the mixture of air and food contents. It was seen in 4 of 11 patients.

4. All but one case showed apparent widening of the cardiac contour on the right. Greater exposure reveals an apparent reduplication of the cardiac contour.

5. In all cases the dilated esophagus, after following the cardiac contour crossed to the left and obliterated the cardiophrenic angle.

In suspected cases complete roentgen studies with barium should be made to differentiate this condition from congenital anomalies involving the esophagus and stomach.

THOMAS F. THORNTON, JR., M.D.

SURGERY OF THE ABDOMEN

GASTROINTESTINAL TRACT

Muñoz, F., Vega, T., Morales, E., Rodríguez, A., and Díaz, A. R. Total Gastrectomy; a Clinical and Physopathological Study *Gastroenterology* 1944, 3 380

Thirteen total gastrectomies were done by the authors during the period from 1941 to 1944 in Mexico. The effects of total gastrectomy are briefly stated following studies on 4 of their patients who survived long enough to be in a good general condition. Comments are made only on results as a whole and the details are omitted. The immediate post-operative mortality was 27 per cent. The total mortality in cases of malignancy was 91 per cent within a period of one and a half years after operation. The average duration of life was ten months. One patient is still living after three years.

The authors consider total gastrectomy for malignancy only in well selected cases. The most favorable lesion is the linitis-plastica type of carcinoma, without metastasis in a middle-aged patient in good general condition. High lesser-curvature ulcers are also suitable for total gastrectomy. Absence of metastatic involvement is necessary. The resection must be total, with the cardia and pylorus visible in the specimen.

The authors are now more pessimistic than they were when they began this type of treatment and believe that the average survival period is not longer than one year which does not sufficiently reward the patient for his effort. In their experience, in general it is advisable to perform subtotal partial gastrectomy for the surgical treatment of cancer.

The physiopathological results in total gastrectomy are shown in table 1 in a review of their 4 cases. The chief disturbance which follows total gastrectomy is motor in character. The general metabolism is preserved and the mineral metabolism is only slightly affected. Anemia may occur especially the hypochromic type. Attention must be given to the diet and pharmaceutical measures to protect the nutrition.

EMIL C. RONTSEK, M.D.

Flemby W. R.: Peptic Ulcer in the Canadian Army (1940 to 1944). *War Med.* Chic., 1944 6 300.

In this report on the dyspeptic syndromes in the Canadian Army gastroduodenal disorders accounted for only 1 per cent of the total admissions to the hospital but they utilized one-eighth of the beds in the medical inpatient division. Only patients with respiratory tract disease were more numerous among hospital admissions.

An accurate diagnosis among recruits was difficult because only fifteen minutes were available for clinical examination. Even with this limited time the per cent of error was only 12 as revised by x ray

study. The length of the history was not always helpful because some patients had very short histories—one being only five days. Psychoneurotics, morons, and malingers made an accurate diagnosis difficult, malingers being the most troublesome.

At first an attempt was made to return men with healed duodenal ulcers to active duty but only 8 of 70 such patients could remain on duty in England. Then an attempt was made "to determine how healed peptic ulcer patients would be able to carry on with some duty in Canada." This study showed that some 10 per cent of these men could remain on active duty. Two factors were important in their ability to do this (1) willingness to continue in service and (2) the ability to select food and environment. It was interesting to note that officers and noncommissioned officers made up half of this group.

Gastric ulcers made up 7 per cent of the total and all of the patients with healed gastric ulcer were unable to continue on duty in England which necessitated ultimate discharge from the service.

From this study the author has concluded that the incidence and significance of peptic ulcer in the army have been overestimated, and that the cause for this is the failure to recognize that military hospitals classify their patients into medical and surgical groups. In addition large outpatient clinics are also conducted. Both parasitic and traumatic illnesses exceed gastrointestinal disease in importance. The author recommends that patients having perforation or hemorrhage be excluded in order to reduce pension responsibility. Moreover, the treatment of peptic ulcer should be undertaken in special units. Segregation of these patients provided a most economical and satisfactory method for their care. The author's final conclusion was as follows: The usefulness of persons suffering from peptic ulceration, whether they are with the armed forces or in civil occupations, is limited. They have a disease which causes serious wastage of man hours and enough misery to warrant the best study possible.

SAMUEL J. FOGELSON M.D.

Hunt G. H., and Bowden J. N.: Rupture of Intestine Caused by Nonpenetrating Trauma of the Abdominal Wall: A Report of Cases. *Arch. Surg.*, 1944 49 331

This report of 6 cases of rupture of the intestine caused by nonpenetrating trauma of the abdominal wall is principally concerned with the results of relatively minor trauma. With the type of injury considered there is likely to be an interval of several hours during which abdominal symptoms are minimal and signs confusing. The symptoms are those of peritonitis, which develop with variable rapidity according to the site of perforation the composition of the leaking intestinal contents and the amount of leakage. Shock is generally not an outstanding fea

ture in these cases but some pain is usually present from the beginning. The two important points are (1) keeping the possibility of intestinal perforation in mind following even minor trauma, and (2) prompt exploration of the abdomen at the first sign of peritonitis. The operative procedure is planned to permit thorough exploration of the entire small intestine since most perforations occur in the jejunum or ileum. If a perforation is found it should be covered with a warm, moist sponge and possible multiple perforations sought.

Six cases are reported in detail. In one of these the intestinal perforation was complicated by other serious injuries which masked the abdominal symptoms and precluded exploratory operation after abdominal symptoms did appear. Another case was accompanied or caused by penetrating trauma. In 4 cases of uncomplicated rupture of the intestine by nonpenetrating abdominal trauma, the mortality rate was 25 per cent in all 6 cases the mortality rate was 33 per cent.

JOHN L. LINDQUIST, M.D.

Spelman, A. E.: Healing of Intestinal Anastomosis. *Am. J. Surg.*, 1944, 66: 309.

The author reports the results of his studies and describes the essentials of the process which establishes continuity of the gastrointestinal tract following either the suture of wounds or an anastomosis. The more common factors causing failure are also presented. The material consisted of pyloric resections, gastroenterostomies, and intestinal anastomoses performed on more than 100 dogs. Serosa-to-serosa approximation by suture was performed on more than 50 rabbits. Varying techniques were used in suturing; some specimens received meticulous aseptic care, others being contaminated with bowel contents. This investigation was further limited to the following procedures: (1) those accomplished without contamination by virulent organisms; (2) those in which unattenuated organisms may produce infected areas; and (3) those attempted in the presence of a deficient blood supply.

Healing was studied after the intestines were sutured with one continuous silk or chromic catgut inverting stitch, including the mucosa, muscularis, and serosa. Another silk stitch included the serosa only.

When the gut wall is inverted by suturing, a triangular chink is formed just outside of the line of anastomosis on the serosal side. Within fifteen minutes fibrillar fibrin begins to form in the exudate which binds the surfaces together and makes them watertight.

During the first few days following the anastomosis there is hyperemia, general edema, and cellular infiltration in the tissues of the sutured area. This leads to tissue which pushes the serosal surfaces into closer approximation, and thus aids in the closing of the chink along the line of anastomosis. The general swelling enlarges the volume of tissue and by its size may produce a brawny thickening of the ring, which causes partial occlusion of the lumen. After a week

the swelling begins to subside and in another ten days it has largely disappeared.

Infection with virulent organisms causes granular fibrin to form. The wound may be temporarily sealed by the granular fibrin but before permanent union of the tissues takes place, it undergoes resolution and the tissue surfaces are freed. The wound then may be easily pulled apart and may leak if the suturing and consistency of the tissue is not sufficient. This dissolution of union occurs most often between the sixth and eighth days.

When the circulation to the stomach was impaired and a posterior Polya type of anastomosis was made in dogs, they recovered from the operation and improved rapidly until, by the fifth day their condition appeared almost normal, then invariably the animals died rather suddenly between the sixth and eighth days.

A study of specimens of this type showed that within twenty-four hours the exudate and fibrillar formation were present, but the latter soon underwent resolution as necrosis developed in the ischemic area.

This study therefore demonstrates that the most tangible aids in establishing a watertight anastomosis were fibrillar fibrin, lack of contamination with virulent organisms, and an adequate blood supply to the area of anastomosis. Every effort should be made to avoid localized areas of ischemia, particularly when the blood supply has already been decreased.

SAMUEL J. FOGELSON, M.D.

Anderson, S. G.: A Statistical Survey of Appendicitis in Children. *Med. J. Australia*, 1944, 2: 597.

An analysis is presented of 933 cases of acute appendicitis treated at the Children's Hospital, Melbourne, between 1931 and 1943. Fifty-five patients were under the age of three years (younger age group) and 878 patients were between the ages of three and fourteen years (older age group).

Complications of abscess or peritonitis were present in 75 per cent of the 55 patients under the age of three years, and in 30 per cent of the 91 patients between the ages of three and six years.

In the younger age group 68 per cent of the patients had temperatures over 102°F., and in the older age group 13 per cent registered fever of this degree. Twelve patients in the older age group with appendiceal abscess or general peritonitis, and 103 patients with acute appendicitis had normal temperatures on admission.

Vomiting preceded abdominal pain in the majority of the patients in the younger age group whereas abdominal pain was the first symptom in the older age group.

Sixty-five per cent of the patients in the older age group were hospitalized for less than ten days, and 32 per cent were in the hospital for more than ten days. Infection of the wounds was the cause of prolonged convalescence in 83 per cent of the cases.

Infection of wounds was studied in 185 consecutive patients in whom this complication occurred,

and in the majority of these (153) there was some degree of peritonitis at the time of operation. Non-purulent fluid was present in the peritoneal cavity in 17 patients, and intraperitoneal drainage resulted in infection of the wounds. This was in contrast to many similar cases in which the abdomen was closed without drainage and without subsequent infection of the wound. In the cases in which there was some degree of purulent peritonitis at operation the smallest percentage of infections of the wounds was noted among the patients in whom the abdomen was closed without drainage—17 per cent of wounds were not infected after intraperitoneal drainage compared to 48 per cent after no drainage.

The mortality figures were as follows:

Children under three years of age	No.	Deaths
Type of Condition		
Acute appendicitis	14	0 (0%)
Acute appendicitis with abscess or peritonitis	41	16 (39%)
Children over three years of age	378	24 (3%)

Twenty two of these deaths occurred in cases complicated by peritonitis or appendical abscess.

In the younger age group a study was made of the mortality in cases complicated by peritonitis or abscess. Of the 11 patients with peritonitis 4 died (36 per cent). There were 18 abscesses, and in one half of the patients the operative technique involved disturbance of the localizing barriers, with 6 deaths (67 per cent); in the remaining half the operative disturbance was minimal (2 appendices not removed) and there were no deaths; the operative findings were inconclusive in the remaining 12 cases.

The influence of sulfonamide drugs as an adjunct in treatment was inconclusive because of the small number of cases in which they were employed.

ERNEST E. ARNHEIM, M.D.

Moreno, I. G.: Transperitoneal Fixation of the Kidney and Colon (Nefrocolonfijación transperitoneal). *Rev. Acad. argent. cir.* 1944, 28: 1063.

The author in collaboration with Russo has operated by the transperitoneal route for fixation of the prolapsed kidney and colon. The patients were between twenty five and thirty years of age and mostly women. Nine of them returned for examination, and a number of pyelograms made before and after operation are shown. The case histories are given. In 90 per cent of the cases all symptoms disappeared. No patient was made worse by the operation. In 50 per cent of the cases there was no constipation before operation, and 90 per cent of the existing constipation in the remaining cases was corrected. Increase in weight after the operation varied from 5 to 13 kgm. Elevation of the kidney was not brought about in 2 cases, but the patients were cured of their symptoms. There was a moderate lifting of the colon in all the cases.

The operations were performed by the technique of Alberto Gutiérrez. It was found, however, that when the quadratus lumborum and psoas muscles

were sutured vertically the muscles tore easily; therefore, they were sutured transversely and to include a large amount of muscle in the suture. Other wise the kidney overcomes the suture and becomes displaced again. The appendix can be removed at the same time as it sometimes plays a part in causing the patient's symptoms. The author believes that more can be accomplished by the transperitoneal route in this condition than can possibly be accomplished by the lumbar route, and that this operation is infinitely superior to any of the other operations proposed for prolapse of the kidney and colon.

AUDREY G. MORGAN, M.D.

Mackenzie, D. H.: Sulfasuxidine in Operations on the Rectum and Colon. *Brit. M. J.* 1944, 2: 722.

Various workers have shown that the administration of succinyl sulfathiazole (sulfasuxidine) causes profound changes in the stools of the recipient, the principal change being a marked decrease in the gram negative organisms of the intestine as shown by colony counts and by the study of films.

In connection with the surgery of the rectum and colon some investigations have been made to determine the action upon the intestinal organisms of sulfasuxidine, sulfaguanidine and sulfathiazole. The technique used was that of Holt and Wright, namely, 0.5 gm. of feces was thoroughly mixed with 4.5 cc. of nutrient broth and serial dilutions were made up to 10^6 . One standard loopful of each dilution was plated on to selective media—MacConkey and desoxycholate citrate agar. Colony counts were made after twenty-four hours at 37°C. Films were examined wet and with Gram's stain.

The author investigated 30 cases. These were studied as follows:

3 cases received 20 gm. per day of sulfasuxidine	
5	10 gm.
8	10 gm. sulfaguanidine
6	2.5 gm. sulfathiazole
8	5 gm.

An account of the results is given. They were remarkably consistent. In the cases receiving 20 gm. per day of sulfasuxidine colony counts and studies of films showed a universal decrease in gram-negative organisms. In cases receiving 10 gm. per day the sterilization was less consistent and more time was required to effect an adequate reduction in gram-negative organisms. The dosage of 5 gm. per day appeared to be ineffective.

The action of sulfaguanidine in no way compared with that of sulfasuxidine, with the exception of the abolition of pathogenic nonlactose fermenters. Even after five or six days' treatment there was frequently a confluent growth of coliform organisms when the 10^4 , 10^5 and sometimes the 10^6 dilutions were plated out.

The use of sulfathiazole as a preoperative treatment has certain obvious disadvantages. It is more likely to cause toxic symptoms than either sulfasuxidine or sulfaguanidine and is far more likely to give rise to renal complications. However even with the

small doses given in these experiments, there was a greater effect than that obtained with sulfaguanidine. There was a decline in gram-negative organisms, and with a dose of 5 gm. per day it was common for bacillus-coli colonies from the 10^2 dilution to number less than 20.

From these studies the author concludes that a dosage of 20 gm. of sulfasuxidine per day for four days before operation as a preoperative treatment, is satisfactory

MATTHEW J. SKIFFERT, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Timoney, F. X.: Cholecystitis. The Advantages of Operative Treatment in Definite Unmistakable Disease. *Am. J. Surg.* 94:5 67:57

Of the 151 patients with cholecystitis treated by the author 90 were female and 61 were male. Seventy-six per cent of the patients were in the thirty to sixty year age group. A reasonably high degree of diagnostic accuracy was obtained. The diagnosis was correct in all but 7 cases. This can be attributed to the presence of x-ray evidence of stone, repeated nonfilling of the gall bladder during cholecystography or the history with symptoms and definite physical signs of an acute attack.

Cholecystectomy was the operation of choice in more than 90 per cent of the cases. Six per cent of the patients required drainage of the common duct. The outstanding indications for common-duct drainage are palpation of stones, a history of jaundice, multiple small stones in the gall bladder with a dilated cystic duct, dilatation of the common duct, and enlargement of the head of the pancreas.

Operations performed in the presence of unmistakable gall bladder disease give assurance of increased satisfactory results. This is the result of more strictly limiting the indications for operation. The presence of gall stones or the history or presence of an acute attack make reasonably certain indications for operation. The operative mortality for unmistakable gall-bladder disease can be kept to a low figure.

SAMUEL KANE, M.D.

Mirizzi, P., and Urrutia, J. M.: Sequelae of Cholecystectomy (Secuelas de la coledocistomía). *Rev. Med. Rio.* 944, 26 501

This is a study of cases in which symptoms recurred after cholecystectomy. It is based on the operations performed by the authors in the past ten years and 1,000 operations performed elsewhere. Graphs show the facts on which their conclusions are based.

They found that cholecystectomy gives complete cure in 95.8 per cent of the cases, and that there are serious sequelae in 1.6 per cent and milder sequelae in 2.6 per cent. Most of the serious sequelae are due to residual stones in the common duct that have been overlooked on operation. Those of lesser seriousness are most frequently caused by spastic disturbance of the sphincter of Oddi and pancreatitis.

Infection is a secondary and not a primary cause of the postoperative symptoms. It aggravates rather than produces the difficulty. Residual hepatitis is not an important factor in causing postoperative symptoms. It generally improves automatically after the cholecystectomy. Adhesions may cause serious sequelae but there are not many cases in which they are the only cause of the disturbance.

Surgical treatment should be complete in the first operation. Repeated operations are always more difficult and dangerous than the first operation. The best means of preventing the overlooking of any stones is by the use of operative cholangiography that is, the taking of roentgenograms of the bile tract during operation. These are much more reliable than roentgenograms taken before operation and make accurate diagnosis possible in 99.5 per cent of cases thus they reduce unpleasant sequelae to a minimum.

ARMSTRONG G. MORSE, M.D.

Schena, A. T.: Rupture of the Common Duct after Cholecholestomy (Ruptura del coledoco postcoledocostomía). *Bol. Acad. argent. cir.*, 1944, 25 390.

Rupture of the scar in the common duct after drainage for infection is rare. Only 5 cases have been described previously in the world literature and the author adds a ninth, on which he operated. The patient was a woman of forty-eight who about a year previously had been operated on for biliary lithiasis, the gall bladder was removed and the common duct drained with a Kehr tube. On the recurrence of symptoms she was operated on by the author and a residual stone was removed from the common duct and drainage again established with a Kehr tube. The tube remained in for a total of thirteen and one half months. Some six months after removal of the tube signs of peritonitis developed and operation showed that infected bile was flowing into the peritoneal cavity from a rupture of the operative opening in the common duct. The pus was encysted, partly because of the presence of adhesions from the former operation and the patient recovered.

The factors that bring about rupture of a cholecholestomy scar are increased pressure within the duct and infection, which softens the cicatricial granulations and makes them friable. There may also be digestion of the tissues from activation of the pancreatic reflex, but there was no history of pancreatitis in this case.

The question of how long a Kehr tube should be left in place after a cholecholestomy is a disputed one. Carter in 1936 published a review of the opinions of North American physicians. Judd said that the tube should remain in place as long as there are any signs of infection and that it does no harm if it remains for months. Schena held that the time should be determined by postoperative cholangiography and the functional tests of Bengtson.

In the discussion Allende said that the probable cause of the rupture was excessive denudation of the common duct during the operation, which deprived the wall of its vessels and led to mortification. This

may occur when it is difficult to free the common duct from a dense inflammatory infiltration and it is particularly apt to occur when a second operation is to be performed as in this case.

AUDREY G. MORAN, M.D.

Martorena, L. H.: Tumor of Vater's Ampulla. Duodenopancreatectomy in One Stage (Tumor de la ampolla de Vater: duodenopancreatectomía en un tiempo). *Boletín Acad. argent. chir.* 1944, 38: 1042.

A safe technique for duodenopancreatectomy with ligation of Wirsung's duct was not devised until 1935. The author describes a case of tumor of Vater's ampulla in a man of forty three who for eight years had had attacks of alimentary intoxication. Followed by a very severe one with intense itching, icterus and acholia he came for treatment. There was a palpable swelling in the right hypochondrium.

Operation showed a lobulated tumor in the head of the pancreas extending back of the mesenteric vessels and connected externally with the wall of the second part of the duodenum. Removal of the tumor after ligation of the vessels, and duodenopancreatectomy with suture of the stump of the pancreas with chromicized catgut were done. The steps of the operation are illustrated. The patient's condition improved under the administration of hypertonic glucose solution, the transfusion of blood and injections of vitamin K. As a substitute for the pancreatic secretion he was given takadlastase and peptopancrease. The pancreatic fistula continued to drain for twenty-seven days and was completely closed forty days after the operation. Histological examination showed adenocarcinoma grade III of Vater's ampulla, adenocarcinoma of the pancreas, and metastatic adenocarcinoma of a retropancreatic gland.

When tumors of Vater's ampulla grow into the lumen of the duodenum they can be removed transduodenally. Among the 126 operations of this kind, 103 were performed before 1935 with a mortality of 33 per cent, and 23 were done since that time with a mortality of 17 per cent. Twenty two of the patients survived three years or more. When the tumor is of the ulcerous type it often invades the inner wall of the duodenum and the head of the pancreas and necessitates duodenopancreatectomy. This operation was formerly performed in two stages but is now performed in one stage when the condition of the patient permits.

The dangers are pancreatic biliary or duodenal fistula and the risks due to the loss of pancreatic juice. The pancreatic fistula often closes spontaneously but if it does not do so in a few weeks the stump of the pancreas should be implanted into the intestinal tract most frequently into the stomach. The biliary fistula shows little tendency to close spontaneously and the best treatment is to anastomose the common duct with the intestine. So far as has been observed from 80 to 85 per cent of the fat ingested is absorbed in man after loss of the pancreas. Definite conclusions as to the effect of the loss of pancreatic juice cannot be drawn until a number of

patients have survived the operation for five years or more.

AUDREY G. MORAN, M.D.

Mirizzi, P. L.: Biliary Lithiasis and Pancreatic Disease. A Contribution on Operative Cholangiography (Litiasis biliar y pancreopatia. Apporte documental de la colangiografía operatoria). *Prensa med. argent.* 1944, 31: 2241.

There is a very close relationship between biliary lithiasis and disease of the pancreas. Among 1,278 cases of acute pancreatitis reported by Schmieden and Sebening there was disease of the biliary tract in 894, or 70 per cent. Statistics reported by other authors give about the same proportion. This relationship is brought about by dystonia of Oddi's sphincter which results in the reflux of bile into Wirsung's duct, or conversely of pancreatic secretion into the bile tract.

Biliary lithiasis is a prominent factor in the causation of acute and chronic pancreatitis and, conversely the reflux of pancreatic secretion into the bile tract is a factor in the etiology of such diseases of the bile tract as perforation of the gall bladder, exfoliative cholecystitis, and biliary peritonitis. It is not the presence of the pancreatic secretion in the bile tract itself that causes the trouble but the fact that it changes the reaction of the bile from acid to alkaline and thus makes it a good medium for activating trypsin to the point where it digests the tissues.

This flow of fluid from the one system to the other can be demonstrated by operative cholangiography that is, the injection of lipiodol into the cystic duct or vestibule followed by the taking of roentgenograms. These demonstrate the reflux.

Cases of the various diseases of the bile tract and pancreas caused by this reflux are described and illustrated.

AUDREY G. MORAN, M.D.

Young, H. B.: A Case of Accessory Pancreas in an Unusual Position Complicated by Acute Necrosis. *Glasgow M. J.*, 1944, 142: 156.

A thirty six year-old male was operated upon for a suspected perforated ulcer. For three weeks he had had midepigastric pain of a stabbing type passing through to the back. This was accompanied by nausea and vomiting. On the day of admission to the hospital he suddenly developed very severe generalized abdominal pain. The abdomen was held rigid.

At operation a firm mass was found in the gastrotrophic omentum along the lesser curvature of the stomach but completely separate from this organ. The mass was the size of a walnut, irregular firm but not stony hard, and unconnected with any other structures. The lesser omental bursa was explored and found to be normal. The pancreas was not unduly hard or irregular.

A biopsy of the tumor mass was proved to contain pancreatic tissue including islets of Langerhans. There were areas of necrosis. The final diagnosis was infection of an accessory pancreas.

EARL O. LATIMER, M.D.

Miller J. M., and Wiper T. B.: Physiological Observations on Patients with External Pancreatic Fistula. *Ann. Surg.* 1944, 70: 852.

During the past ten years there have been only rare reports appearing in the medical literature of physiological observations made upon human subjects with external pancreatic fistula. The fundamental information concerning pancreatic function has been derived from the experimental laboratory animal, on which with painstaking care the fundamentals of pancreatic secretion have been investigated. Rarely has the clinician been given the opportunity to correlate the physiological observations made upon the human being with the results obtained from the experimental animal. The recent advances made in the operative attack upon lesions of the pancreas make it imperative that the surgeon be more conversant with the physiology of that organ for interference with the normal flow of the external secretion will result in profound alterations in the total metabolism.

A rare opportunity was offered to make observations on the influence of such persistent fistulas upon these patients, particularly with reference to the many alterations induced. The observations included

- (1) the general nutritional state of the patient
- (2) the total pancreatic flow in twenty-four hours
- (3) the pattern of flow in a twenty-four-hour period
- (4) the plasma-electrolyte pattern
- (5) the plasma protein
- (6) the influence of water intake on the pancreatic flow
- (7) the observations on volume flow alterations induced by the administration of various substances into the duodenum
- (8) the effect of intravenous fluids upon the pancreatic secretion and
- (9) observations on volume flow alterations induced by the subcutaneous administrations of drugs.

They are reported in detail in a statistical study presented in this article.

Pancreatic flow is continuous throughout the twenty-four hour period and is influenced, to great degree, by the state of hydration of the individual. One pancreas produced 1,770 cc. of fluid in a twenty-four-hour period. Attention was drawn to the marked alteration in water balance plasma-protein level, and plasma electrolytes, with special emphasis upon plasma sodium in patients with severe external pancreatic fistula. It was emphasized in this presentation that the sodium loss in severe pancreatic fistula produces a clinical syndrome similar to that described by Addison, with the exception that adrenal disease is not present. This analogy has not been stressed previously. The administration of adequate amounts of sodium and water in the presence of sufficient plasma protein to hold them in the circulation alleviates the symptoms peculiar to this syndrome.

Diminution in pancreatic secretion through the fistula may be obtained by the administration of a number of drugs. However ephedrine and sodium bicarbonate are the most practical of these because of the unpleasant or deleterious side-effects of the

others. Pancreatic secretion is markedly stimulated by the intramuscular administration of histamine, and by the intravenous administration of physiological saline solution or 5 per cent glucose in physiological saline solution.

Detailed physiological observations upon pancreatic function were recorded. Certain of these observations contribute definite support to the theory that secretin secretion is a filtration process. These are

1. Sodium ion is present in equal amounts in both blood plasma and pancreatic secretion.
2. The total of the concentrations of chloride and bicarbonate ions are the same in blood plasma and pancreatic secretion.
3. The same amount of ionizable calcium is present in blood plasma and pancreatic secretion.
4. Sulfanilamide is found in the same amount in blood plasma and pancreatic secretion.

Large amounts of ionizable calcium are normally returned to the gastrointestinal tract through pancreatic secretion. This phenomenon has not previously received the recognition it warrants.

The appearance of sulfanilamide in therapeutic concentration in pancreatic secretion suggests its use in acute inflammatory disease of the pancreas.

JOHN E. KIRKPATRICK, M.D.

Erb, W. H.: Radical Pancreatoduodenal Resection for Adenocarcinoma of the Head of the Pancreas. *Surg. Clin. N. America*, 944, 24: 1370.

The development by Whipple, Brunschwig, and others of a surgical technique for the radical removal of carcinoma of the head of the pancreas necessitates an earlier diagnosis so that more and more cases may be found to be operable at laparotomy. With this in mind, the author charted laboratory data, histories, symptoms, and physical signs to aid in the differential diagnosis of surgical and nonsurgical jaundice of the hepatocellular variety. The diagnosis of hemolytic jaundice is usually sufficiently clear, and it is not included in the tables. If a definite diagnosis cannot be made, then surgical exploration is indicated. If the lesion is not surgical the harm to the patient can be kept at a minimum with adequate preoperative preparation and continuous spinal anesthesia.

A woman, aged fifty-two years, had been well until a year before admission, at which time she began to complain of vague indigestion and gas pains. There was no recent history of jaundice or of pruritus. The Graham-Cole test sixteen hours after oral administration of dye failed to show any evidence of a gall bladder shadow. The patient's clinical history and the presence of a small extrinsic pressure defect on the duodenal cap aroused the suspicion of early malignancy of the pancreas or common duct. Examination at this time revealed a mild icterus and a palpable mass in the region of the gall bladder. The Van den Bergh test was immediately direct, the icterus index 30 units, and the quantitative serum bilirubin 1.4 mgm. per 100 cc. of serum.

Under continuous spinal anesthesia, a laparotomy was done through a right rectus incision. A greatly distended gall bladder and common duct were exposed. A mass which appeared movable was felt in the head of the pancreas. The distended gall bladder interfered with exposure therefore it was drained of normal-colored bile. A radical resection in one stage was decided upon. The stomach was divided proximal to the pylorus and closed. The duodenum was fixed and divided 5 cm. distal to the lesion. The common duct was isolated, ligated, and divided. The closure was reinforced by interrupted sutures of silk. The body of the pancreas was then bisected 3 cm. from the lesion. Two distended ducts were separately ligated and the pancreas was turned in with silk.

The head of the pancreas was markedly adherent to the portal vein and had to be freed from it by sharp dissection. The jejunum could not be brought in contact with the gall bladder without tension, probably because of the marked scoliosis, but as the distal end of the duodenum was readily available the author made an anastomosis between the gall bladder and the duodenum. Silk was used for the serosal layer and catgut for the mucosal, in all the anastomoses. Following this a routine retrocolic, posterior gastrojejunostomy was done. Two cigarette drains were placed next to the bisected pancreas and brought out through a stab wound. The peritoneum was closed with catgut the anterior rectus sheath with catgut and tension sutures of wire, and the skin with wire. The patient received 500 cc. of blood and 800 cc. of normal saline solution on the table.

The pathological report was adenocarcinoma of the pancreas.

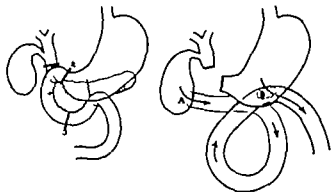


Fig. 1. Left, Schematic drawing showing points of division as described in the operative note.

Fig. 2. Schematic representation following anastomosis. The pancreas and transverse colon are not shown for the sake of clarity.

The postoperative course was smooth. Starting on the third postoperative day and lasting until the twelfth postoperative day there was profuse drainage from the stab wound of what was assumed to be pancreatic juice. No bile was ever noted in this drainage. The patient was discharged from the hospital on her twenty third postoperative day.

The author concludes that permanent cure of carcinoma of the head of the pancreas will follow the successful resections only rarely. The anatomic position of the pancreas adjacent to vital structures (portal vein) which cannot be sacrificed prevents one from doing a wide resection of the growth. However life expectancy can be increased as in this case in spite of the fact that the pathologist found the tumor at the very edge of the resected tissue.

JOSEPH K. NARAT, M.D.

GYNECOLOGY

UTERUS

Chaffin, R. C.: *Procidentia. The Chaffin Vaginal Subtotal Hysterectomy for the Cure of Fourth Degree Prolapse; Review of Technique and Results.* *Am. J. Surg.* 1944, 66: 338.

The author prefers the Watkins-Wertheim interposition operation for the correction of cystocele associated with minor degrees of uterine prolapse. He describes an operation devised to remedy more severe grades of prolapse associated with uterine, bladder and cul-de-sac protrusion. The cervix is treated with the Percy cautery if indicated. A supracervical hysterectomy is then performed by the vaginal route, and the severed ends of the round and broad ligaments are sutured into the lower posterior surface of the cervix or into the cul-de-sac itself. The retained cervix is sewn to the pubovaginal fascia to obliterate the opening through which the bladder protrudes and the operation is completed with a perineorrhaphy.

GROVER BUNNEX, M.D.

Macfarlane, C., Sturgis, M. C. and Fetterman, F. S.: *The Value of Periodic Pelvic Examination in the Control of Cancer of the Uterus.* *J. Am. M. Ass.* 1944, 65: 877.

A group of presumably well women between thirty and eighty years of age volunteered to come for pelvic examination twice a year for five years to test the value of periodic pelvic examination in the control of cancer of the uterus. A total of 9,111 examinations have been made. 545 volunteers have completed the five-year period.

In the course of these 9,111 examinations, 4 early cancers of the cervix and 1 early cancer of the uterus were discovered. The patients were adequately treated. They remain well, 3 for six years, for five years, and 1 for fifteen months after treatment.

Also in the course of the 9,111 examinations, 461 inflammatory lesions of the cervix were discovered. Two hundred of these have been treated and eliminated.

GROVER BUNNEX, M.D.

Ingraham, C. B., Black, W. C., and Rutledge, E. K.: *The Relationship of Granulosa-Cell Tumors of the Ovary to Endometrial Carcinoma.* *Am. J. Obst.* 1944, 48: 766.

Granulosa and theca-cell tumors may be associated with such excessive and abnormal endometrial hyperplasia that a histological pattern indistinguishable from adenocarcinoma results.

In further investigation of this question the authors studied a series of 6 hysterectomy specimens, including the ovaries, in corpus carcinomas, in order to determine whether or not hyperplasia of ovarian stroma, interstitial cells, or follicular lining cells was associated with carcinoma. This study

showed no constant relationship, and it was found that the ovaries were either partially or completely atrophic in all instances. The amount of deeply basophilic mesodermal tissue present in the ovarian stroma and not demonstrably connected with follicular structures was variable, and while a considerable amount of this tissue was present in some cases, there was almost a total lack of it in others. A further series of 15 corpus cancers was studied for histological comparison with endometrial hyperplasia associated with granulosa-cell tumors.

Examination of such specimens provided an opportunity for comparison of the growth characteristics of corpus carcinoma and the condition of excessive proliferation caused by granulosa-cell tumor.

The most important features of corpus carcinoma are its progressive growth with continuous and irreversible proliferation with invasion of the myometrium and establishment of metastases. Some of these features are lacking in many true carcinomas and in all reported cases of excessive hyperplasia, including the authors.

Two additional cases of granulosa-cell tumor and 1 case of theca-cell tumor of the ovary associated with adenocarcinoma of the corpus uteri are reported.

EDWARD L. CORRELL, M.D.

Peralta Ramos, A. G., and Gramajo, G.: *Immediate and Late Results of the Wertheim-Schauta Operation (Resultados Inmediatos y Alejados de la Operación de Wertheim Schauta).* *Obst. ginec. Mex.* 1944, 3: 766.

Genital prolapse is frequently accompanied by retrodeviation of the uterus. The operation for the correction of these conditions was formerly performed in two stages, a vaginal and an abdominal one. However, it has been found advantageous to suppress the abdominal stage and operate entirely through the vagina. The Wertheim-Schauta operation fulfills this requirement. It interposes the uterus between the bladder and the anterior wall of the vagina, which occludes the vagina and permits the uterus to act as a support for the bladder. The chief indication for the operation is found in cases of prolapse of the second degree with a large cystocele and incontinence of urine. It is a simple operation and easily accomplished under local anesthesia. The vaginal flora should be studied in determining its indications, and it should be supplemented by the local intraperitoneal use of a sulfonamide. It should be used only for women at or near the menopause as pregnancy under the anatomical conditions created by it is dangerous.

The authors give the histories of 38 patients on whom they have used this operation. Fourteen of them returned for later examination and of these 11 or 78.5 per cent, were permanently cured, while 3 or 21.43 per cent had a recurrence. It is a good

operation for genital prolapse provided it is performed on the proper indications. North American physicians call this Watkins operation as they claim that the first interposition operation was performed by Watkins in 1898.

Recurrences are generally caused by elongation of the cervix, and to prevent them Wagner recommends amputation of the cervix during the operation and Wertheim proposes fixing it to the uterine ligaments.

AUDREY G. MORRAN, M.D.

ADnexAL AND PERIUTERINE CONDITIONS

Rabin, I. C. Novak, J. and Squire, J. J.: Ovarian Fibromas and Theca-Cell Tumors. Report of 78 Cases, with Special Reference to the Production of Ascites and Hydrothorax (Meigs Syndrome). *Am. J. Obst.*, 1944, 48: 601.

The first group of tumors reported from 1928 to 1936, consists of 23 cases. In 7 the tumors were small, measuring at most 5 cm. in 10 cases they were of medium size, from hen-egg to apple size and in 5 cases they were large, bigger than an average sized grapefruit. In 1 case there was no definite note as to size. Ascites was observed in 9 cases of this group. In 2 cases the amount of fluid was small, in 3 moderate, and in 4 considerable. In 6 cases with ascites, the tumors were of large size and in 3 they were of medium size. In 7 cases, the tumors were edematous and for the most part, cystic in 2 cases they were hemorrhagic. Hydrothorax was found in only 1 case of the group. The pleural effusion was bilateral and much more pronounced on the right side than on the left. It was hemorrhagic, whereas the ascitic effusion was described as amber colored. This unusual circumstance is not explained by the authors.

The second group of tumors consisted of 30 fibromas (including fibromyomas), 2 papillary fibroadenomas, and 23 theca-cell tumors. This fairly large group indicates incidentally that theca-cell tumors are not as rare as has been generally assumed. Three of the fibromas were large, 14 of medium size and 13 small. There was a small amount of ascites in only 2 of the fibroma cases. The relative infrequent occurrence of ascites in this group is difficult to explain. In 1 of the 2 cases of papillary fibroadenoma a small amount of ascitic fluid was found at operation. Hydrothorax was not found in any of these 30 cases of ovarian fibroma.

Among the 23 cases of theca-cell tumors, ascites was noted 7 times. The abdominal effusion was extensive in 3 cases with large tumors. A hydrothorax on the right side was associated with the ascites in 1 case. In 4 cases with a moderate amount of ascitic fluid, the tumors were only of medium size, i.e., from that of a hen's egg to that of a grapefruit. In 6 cases with ascites, the new growths were edematous, and in 4 cases cystic.

Ascites is not a frequent occurrence in ovarian fibromas if one considers all of the fibromas including the small ones.

Ascites as well as the combination of ascites and hydrothorax (Meigs syndrome) is also found in theca-cell tumors.

The ascitic fluid probably originates from the tumor itself. Gelber's observation on the oozing of fluid from an ovarian fibroma placed in a dry vessel should be verified. The conditions which may bring about a lymph congestion in the tumor should be studied by a thorough examination of the lymph and blood vessels in the tumor tissue in the pedicle and on its surface.

In every case of Meigs syndrome the specific gravity, the albumin and cell content and the osmotic pressure of the ascitic and pleural effusions should be determined.

The anatomic routes by which fluid is transferred from the peritoneal into the pleural cavity are described. Living cells, cell debris or chronic inflammatory changes of the peritoneum or of the pleura may block the connections between these two cavities.

The prevalence of pleural effusions on the right side can be explained by anatomic and physiological conditions, i.e., the better development of the diaphragmatic lymph channels, the higher position of the diaphragmatic dome and the more intensive pumping action of the diaphragm on the right side.

A hydrothorax can best come about not only if the ascitic fluid is poor in colloids, and therefore can easily pass the diaphragm, but also if the absorption and deportation of the fluid is not rapid enough in the pleura to prevent its accumulation.

EDWARD L. CORNWELL, M.D.

MISCELLANEOUS

Miller, H. E.: Deaths in Gynecology. *Am. J. Obst.* 1944, 48: 834.

The general impression received from a study of 401 deaths (two-thirds of which were due to malignancy) is that, on the whole, the cases were well managed from the standpoint of the hospital and that in the great majority of cases (particularly the malignancies) after due allowance is made for the speed and general hopelessness of such conditions as adenocarcinoma of the ovary the patients were responsible for their own deaths. On the other hand in perhaps 25 per cent of the cases with death from malignant disease the patients might have been given a chance of life and in perhaps half with death from benign disease the outcome might have been different if the plan of management outside as well as inside of the hospital had been different in some or in all respects.

Ectopic pregnancy was the cause of the death of 15 patients, 9 of whom were not submitted to surgery. This is a truly startling situation for of all emergency gynecological conditions, none responds more promptly and more satisfactorily to surgical therapy than ectopic pregnancy. Histories should be taken with much more care from every standpoint.

There should be less complacency about the risk in both uterine fibroids and pelvic inflammations. In this series, the responsibility for the cases in which there was an unwise estimation of the risk was about equally divided between the surgeon and the medical consultant.

In all surgical cases there could well be a more careful evaluation of the need for preoperative therapy even when the patients seem fair risks and present only minimal deviations from the normal. Blood surveys should be carried out in all cases, and mild degrees of anemia, hypoproteinemia, urinary tract disease, and hepatic dysfunction should be investigated.

There should be more alertness after operation to detect possible complications in their incipency more speed in instituting treatment when such complications are discovered, and a quicker resort to such measures as intestinal decompression, infusion transfusion, and oxygen therapy when it is evident that less active measures are not achieving results.

More discretion should be employed in discharging patients in certain categories without adequate provision to bring them back if they do not return voluntarily as directed. A fair number of women with malignant disease in this series signed their own death warrants because, when they improved after irradiation which was well begun, they failed to return for more. Patients with pelvic inflammations who responded to bed rest often delayed likewise.

Patients with obvious abscesses, among whom the proportion of rupture was startlingly high, should be kept under observation in the hospital and should be

operated on promptly when maximum improvement is evident, or when it is clear that no further improvement can be expected.

A more general use of total hysterectomy would automatically prevent the development of a certain proportion of cases of malignancy of the cervix.

It should never be forgotten that a patient with one disease even if that disease is malignant, may have or develop another disease even a malignant one at the same time. Pelvic examination should be made a routine part of all physical examinations. A much higher "index of suspicion" of malignant disease, and especially of malignancy of the cervix, must be ingrained in medical students, interns, and residents. Interns and residents, in particular must be imbued with the belief that not all instances of malignant disease are hopeless, an idea which a surprising number of them now seem to possess, and which results in an eager desire to clear the wards of such cases and to use the beds for other purposes. For frank errors of diagnosis and treatment we are responsible as individuals, and most of the preventable deaths from benign disease in this series fall into that classification.

As many of these cases show the menopausal years are a period of particular danger in a woman's life because of the possible confusion between the expected irregularities of those years and the early symptoms of malignancy of the cervix. The solution would seem to lie in teaching women to submit to pelvic examination at regular intervals whether or not they present symptoms.

EDWARD L. CORNELL, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Ayre, J. E., and Kearna, P. J.: The Course of Pregnancy Following Total Ovarian Ablation
Canad. M. Ass. J. 1945 52 24.

The authors report a case of removal of an ovarian cyst in a patient two and one-half months pregnant whose other ovary had been previously removed. Following the operation from the sixty third to the eighty third day of pregnancy the urine pregnandiol readings were zero consistently but they later increased to a high of 189. The pregnancy advanced normally until about five months at which time it terminated spontaneously.

The period during which no pregnandiol was excreted probably represents the interval between the removal of the corpus luteum and the assumption of the function of hormone production by the placenta.

J. ROBERT WILLIAMS, M.D.

Williams, P. F. and Corbit, J. D.: An Analysis of 161 Fatalities from Ectopic Pregnancy
Am. J. Obst., 1944, 48 841

In Philadelphia, among 2204 ectopic gestations recorded by the hospital record librarians and the Coroner's office from 1931 to 1943 inclusive there were 101 deaths, a mortality of 4.6 per cent.

This study presents a review of these fatalities and attempts to fix responsibility for the deaths, and to seek out the avoidable factors.

The responsibility has been found to be divided between the patient and her family, the referring physician and the attending surgeon and his hospital staff. The avoidable factors have been found to include lack of education of the lady regarding early and adequate prenatal care, failure of the referring physician in recognizing the possibilities of differential diagnosis, failure on the part of the surgeon in diagnosis and because of delay in operating, lack of transfusion, and poor choice of operative procedure.

EDWARD L. CORKILL, M.D.

Crabtree, E. G.: The Use of the Sulfonamides in Pylonephritis in Pregnancy
J. Am. M. Ass. 1944, 126 810

According to the author sulfonamides have greatly modified the management of pylonephritis in pregnancy. There is a definitely good effect which will make itself apparent promptly as a rule. Patients who show signs and symptoms of pylonephritis in pregnancy were given 2 gm. daily of sulfathiazole or sulfadiazine for six days. Sixty grains of sodium bicarbonate are also given three times daily while the patients are receiving the sulfa drugs. The fluid intake is between 2500 and 3000 cc. of water daily in addition to other fluids in the diet. This routine is followed with outpatients. Whenever patients are febrile they are hospitalized and the routine is more

varied. Alkalinization, forcing of fluids, and sulfathiazole are the basic items in the treatment of these patients.

All patients treated are relieved of symptoms although the patients are not all cured.

All obstetrical patients with pylonephritis should be given a course of sulfonamide therapy and if the infection is not cleared up by this they should be investigated for lesions of the urinary tract.

Cystoscopy is used more for diagnosis than for its therapeutic effect. Many patients are discharged from the hospital with infected urine and no symptoms. This may cause preventable gross damage to the urinary tract after long or repeated injuries. Therefore, it is important to realize that subsidence of symptoms following sulfonamide therapy does not mean cure. Patients should be checked carefully after pylonephritis is diagnosed and followed up for some time thereafter.

HARRY FIELDS, M.D.

Flinn W. F.: Lymphogranuloma Venereum in Pregnancy
Am. J. Obst. 1944, 48 696

The author briefly reviews 11 cases of lymphogranuloma venereum in pregnancy from the New York Lying In Hospital. Patients with this disease are usually colored and they are almost invariably syphilitic therefore when one encounters such a patient with a rare venereal disease one can almost infer that she will have a more common venereal disease. These patients are frequently anemic.

As to the type of delivery a vaginal examination before the onset of labor or in early labor will give the most information. If there is marked perineal fibrosis, soft tissue masses or fixation of the posterior vaginal wall, vaginal delivery will be fraught with difficulty and danger.

It is interesting to note that in both of the cases of rupture of the rectum, breech extraction was performed. Hence, when a breech presentation is found in a woman with a stricture of the rectum external cephalic version should be attempted.

One colored patient (a para iv and gravida vi), after a three-hour first stage and a one hour second stage of labor, developed a semicircular rupture of the uterus. She was operated upon and recovered. She also had syphilis. EDWARD L. CORKILL, M.D.

LABOR AND ITS COMPLICATIONS

Morgan, J.: Report on 130 Consecutive Cases of Placenta Previa without Maternal Death
J. Obst. Gyn. Brit. Empire 1944, 51 509.

The author reports a consecutive series of 130 cases of placenta previa without a maternal mortality and with a fetal mortality of 22 per cent.

Of the 130 placentas 32 were implanted centrally, 46 were marginal and 52 were lateral. Treatment was as follows:

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- Central placenta previa (32 cases)
 - Cesarean section
 - Application of Willett's forceps
 - Manual removal of the placenta before delivery of the infant when the patient was admitted fully dilated
- Marginal placenta previa (46 cases)
 - Cesarean section
 - Application of Willett's forceps
 - Pulling with the half-breach
 - Artificial rupture of the membranes
 - Normal delivery
- Normal placenta previa (52 cases)
 - Cesarean section
 - Application of Willett's forceps
 - Artificial rupture of the membranes
 - Normal delivery
- Other deliveries were required in 16 cases. The causes of fetal death were:
 - Prematurity
 - Congenital atelectasis
 - Cerebral hemorrhage
 - Congenital defects

J. ROBERT WILLIAMS, M.D.

MISCELLANEOUS

- Dempsey, E. W., and Wietlocki, G. B.: Observations on Some Histochemical Reactions in the Human Placenta, with Special Reference to the Significance of the Lipoids, Glycogen, and Iron. *Endocrinology* 944, 35 409.

The authors describe some interesting histochemical reactions in the placenta. These are concerned chiefly with lipoids, glycogen, and iron. The material for study consisted of 9 human placentas of various ages, the youngest coming from an embryo 3 mm. length. Some of the placentas were fixed in various reagents for special cytological study while others were studied fresh and unfixed.

The types of study included fluorescence studies, transillumination with ultraviolet rays, and birefringence with a polarizing microscope. The Schiff, or "plasmal," reaction of Penzance and Voit was used to study aldehydyl compounds, and strong sulfuric acid was applied to fresh and formalin fixed tissues to determine the localization of sterol-like substances. Best's carmalum stain was utilized to locate glycogen. The oxidative systems of the placenta were studied by means of the application of "nadi" reagents and their ability to oxidize or reduce a series of indicator dyes.

The conclusions reached by these observers are that lipoids of the fetal placenta occur almost entirely as droplets in the syncytial trophoblast. These droplets contain steroidal substances. The cytotrophoblastic cell columns, cell islands and cytotrophoblastic shell contain glycogen, especially during the early part of pregnancy. Similarly, a considerable amount of glycogen is present in the decidua in the first half of pregnancy. The authors suggest from their conclusions that glycogen deposition is

associated with anaerobic conditions, and that through anaerobic breakdown a mechanism for oxidative reactions of tissues in which the oxygen supply is deficient is produced. They also concluded that the syncytium of early placentas contained a considerable amount of iron, while in the later stages of pregnancy this amount is greatly reduced. These findings are interesting with regard to iron transport by the placenta.

HARRY FRANKS, M.D.

- Aravena, O.: Maternal Mortality from Obstetrical Causes in Chile (Sobre mortalidad materna por causas obstetricas en Chile). *Bolet. Soc. chilena obst. ginec.* 1944, 9 179.

The author gives tables which show the maternal mortality from obstetrical causes in Chile from 1919 to 1943. The causes of death are also tabulated and the statistics are compared with those of other countries. Part of the statistics were obtained from the Government Statistical Bureau and part from various hospitals, and attention is called to the differences for the differences in the government and hospital statistics. The author believes that the best way of calculating such statistics is to count the number of maternal deaths to every 10,000 infants born alive. The arguments for and against the various methods of computing statistics are set forth.

The author finds with regret that there has not been a decrease in the maternal mortality in Chile within this period comparable with that in other highly civilized countries. In the United States there has been a rapid decrease in maternal mortality since 1930. In England and Wales there has been some improvement in the last decade while in Norway and the other Scandinavian countries the figure is very low.

He attempts to explain the backwardness of Chile in this respect. Chilean physicians know the most modern medical and surgical methods of management of delivery and the puerperium. However, the infant seems to be in the fact that the mass of the population is not made available to a medical question. It is a social as well as a medical society devoted to the investigation of the causes of maternal mortality and a detailed study of each case of death, while in Chile there is no such activity. Chile should organize early and compulsory prenatal control, and pregnant women should be under medical observation and care from the beginning of pregnancy. Medical and scientific societies should accept the responsibility of bringing about better obstetrical care for the mass of the population.

In the discussion the facts were brought out that it is difficult to lower the maternal mortality until induced abortion with its high percentage of sepsis can be controlled and also that the highest mortality in Chile is in the country districts where the skilled medical care of the cities is not available.

ARMANDO G. MORALES, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY AND URETER

Dermady E. M. Siddons, A. H. M., Corson, T. C. Langton, C. D. and Others: Traumatic Uremia; Reports on 8 Cases. *Lancet*, Lond., 1944, 247 809.

Six fatal cases and 3 nonfatal cases of uremia which occurred in young soldiers a few days following injury by high-explosive missiles are reported. The injuries were severe but in themselves did not seem sufficient to cause death. All of the men developed oliguria, vomiting and a raised blood urea. Many of them had a low blood pressure and were in clinical shock at one time during their illness. Pathological examination of the kidneys in 4 cases coming to autopsy revealed enlargement of the kidneys with histological evidence of tubular degeneration, interstitial edema, and rupture of the tubules into the venous spaces.

The similarity between the pathology of this syndrome and the crush syndrome is great. The renal changes are probably due to anoxia secondary to hypotension or vascular spasm or both, and are probably not due to 'nephrotoxic' substances liberated from crushed tissues as there was little crushing present in these cases. These 6 fatalities represent one-third of the deaths in a group of 2,000 casualties which were observed in a transit air evacuation hospital in northern France.

WILLIAM W SCOTT M.D.

Dean, A. L., and Abels, J. C.: Study by Newer Renal Function Tests in an Unusual Case of Hypertension following Irradiation of One Kidney and Relief of the Patient by Nephrectomy. *J Urol*, Balt., 1944, 52 497.

The measurements of renal function commonly employed by urologists such as the determination of blood nonprotein nitrogen and urinary concentration and the dilution tests, do not always measure accurately the amount or nature of renal damage and provide still less information of the reserve capacity of the organs.

A case illustrative of the value of the newer renal function tests is presented. At the age of twenty years a woman complained of an abdominal mass of six weeks duration. Except for the mass, physical and laboratory examinations were normal. Urograms were normal. Under a diagnosis of lymphosarcoma or Hodgkin's disease 3,000 roentgens were administered through anterior and posterior portals, and it was calculated that the kidney received 4,600 roentgens. The tumor disappeared completely but seven years later the patient's blood pressure was 150/100, and when headaches began to appear it was found to be 184/125. Excretory urograms showed a shrunken left kidney with diminished function. The usual tests showed little impairment of

the left renal function but when the rate of glomerular filtration was measured by the mannitol clearance technique it was found that the left kidney cleared only 17 ml./min. The renal blood flow as determined by the sodium para-aminohippurate method was 410 ml./min. for the right and only 70 ml./min. for the left kidney. Maximum tubular secretion of this compound was shown to be 50 mgm./min. on the right side and 6 mgm./min. on the left side.

Following removal of an atrophied left kidney the blood pressure fell from 160-172/120-130 to 112-120/72-80 within one week. During the following fourteen months the blood pressure remained in this range and renal function tests showed slight improvement in the function of the remaining kidney. Vascular responses to cold and nitroglycerin which were poor preoperatively became normal and the venous pressure and circulation times decreased to normal values following operation.

It is suggested that when it is important to determine the functional capacity of a kidney use of the newer tests of renal function be made as the present function tests are frequently inaccurate and are not sufficiently sensitive to detect renal damage.

WILLIAM W SCOTT M.D.

Deming, C. L.: Acute and Chronic Symptoms and the Diagnosis of Movable Kidney. *Pennsylvania M J*, 1944 48 207.

Although mobility of the kidneys is normal, in some adult females it causes pain presumably because of temporary obstruction of the pelvis of the kidney. Pain, the most common symptom of pathologically movable kidneys, is usually referred to the corresponding costovertebral angle although gastrointestinal complaints and nervous symptoms may predominate. In a certain proportion of the cases hydronephrosis is present and impaired renal function and delayed emptying of the renal pelvis are the late effects of pathologically movable kidneys. Treatment of 200 selected cases by suspension of the kidney resulted in failure to relieve the symptoms in only 4 cases.

The author mentions the fact that the Kelly stitch operation and capsule-stripping operations for nephropexy should be avoided because of the danger of perinephritis and hypertension. The author's nephropexy consists of complete mobilization of the kidney pelvis, and ureter, the kidney being placed in its correct position and the anterior and posterior layers of the perinephric fascia being approximated with chromic mattress sutures to maintain the kidney in normal position. Nephropexy may be indicated following pyelolithotomy or plastic operations on the renal pelvis to maintain the normal position and emptying of the pelvis of the kidney.

DONALD F McDONALD, M.D.

Crabtree E. G.: Leiomyoma of the Kidney Associated with Hemorrhagic Cyst. *J Urol*, Balt., 1944, 5: 450.

Tumors which arise from smooth muscle tissue and are situated beneath the true capsule of the kidney are usually small, multiple, benign fibromyomas and usually do not require surgical treatment. Myomas of the kidney have grown to larger size, produced symptoms, and assumed surgical significance in a very small number of reported cases. Of 8 reported cases of renal myomas of large size only 3 were histologically malignant. The benign myomas have a tendency toward cyst formation both in association with the tumor and within it. Of the 6 reported benign myomas 3 were accompanied by cyst formation, whereas the 3 malignant myomas lacked cysts. In the cyst wall, encrustation with cholesterol or calcium was the rule. Both benign and malignant tumors have been found well encapsulated within the renal capsule. Results of nephrectomy for renal myoma are good no doubt because extension into the perirenal fat and veins does not occur. Of the 8 tumors recorded 6 have been in women. The age incidence of renal myoma is from twenty-one to fifty-two years with 7 patients under thirty-nine years.

Two cases of renal myoma are presented. One was benign and occurred in a male aged thirty-nine years whose initial complaint was loin pain and who has remained well for six months. The other was malignant and occurred in a forty-three-year-old woman who complained of a left abdominal mass. Following nephrectomy it recurred in three years and was again removed then it recurred in two years at which time further surgery was instituted.

In the first case the tumor was a thick-walled cyst 5 cm. in diameter the wall of which contained calcification and whorls of smooth muscle and connective tissue without evidence of malignancy. In the second case the tumor was 16.5 cm. in diameter and was not cystic. Microscopic examination showed connective tissue, smooth-muscle cells, and numerous mitoses which led to the diagnosis of leiomyosarcoma.

Until greater familiarity with the clinical appearance of leiomyomas of the kidney is attained pathological examination of the specimen removed by nephrectomy should be regarded as the only reliable method of establishing the malignancy or benignancy of the tumor.

WILLIAM W. SCOTT, M.D.

Sugarbaker E. D.: An Application of Staging in the Removal of Difficult Wilms Tumors. *Ann. Surg.* 944, 30: 90.

Mixed tumors of the kidney occur most frequently in infancy and early childhood. They are characterized by rapid growth to large size and early metastases to the lung and liver and have a quickly fatal termination.

Roentgenotherapy either alone or as a preoperative adjunct is much inferior to immediate nephrec-

tomy. A transperitoneal approach is desirable because it permits of the intact removal of the tumor and the perinephric fat within the fascia of Gerota. Another advantage of this approach is that it permits primary ligation of the renal pedicle before the tumor is disturbed, which is desirable because of demonstrable renal vein involvement in 45 per cent of the cases.

Operability of these tumors depends not only upon the presence of metastases but also upon the technical ability of the operator and the size and position of the tumor. Operability may be extended by dividing the operation into two stages to minimize the risk and to facilitate the excision of the bulky very vascular tumor. Ligation of the pedicle of the kidney and mobilization of a portion of the tumor at the first stage permits of rapid excision with less bleeding at the second stage. The kidney and tumor should be removed intact with the perinephric fascia and fat and the overlying peritoneum.

A case of mixed tumor of the right kidney in a twelve-year-old boy in which a 1,760 gm. specimen was removed by the two-stage procedure described is presented in detail. The stages were six days apart, and the patient is in good condition two years after operation without evidence of recurrence.

DONALD F. McDONALD, M.D.

McClelland, J. C.: Primary Carcinoma of the Ureter Treated by Excision and Anastomosis of the Cut Ends. *J Urol*, Balt., 1944, 51: 5.

A man, aged sixty-two, noticed two weeks before consultation that there was some blood in the urine after walking. The blood was intimately mixed with the urine, and he noticed a few small clots. There was no frequency, no pain, and no difficulty in urination. He gave a history of having passed 3 stones from his left ureter two years ago. There was an indefinite area of pain in the left lower quadrant, but none in the right lower quadrant.

Under local anesthesia a No. 24 F. cystoscope was introduced and clear urine was found in the bladder. The vesical mucosa throughout was pale pink in color and showed no stone, tumor, or foreign body. No intravascular enlargement of the prostate was present. The ureteral orifices were examined and no efflux was seen coming from either side. A catheter passed up the left ureter did not meet any obstruction. The right ureter was not catheterized as the patient had had his pain on the left side previously and the author suspected a recurrence of ureteral stone. The left pyelogram was negative for calculus or any abnormality in the pelvis or ureter.

An intravenous pyelogram showed a right hydronephrosis with a kinking of the upper ureter. The cystoscopic examination was repeated and a stricture in the lower end of the right ureter, a kink at its upper end, and an incompletely filled hydronephrosis were found. A tentative diagnosis of new growth in the lower end of the right ureter was made and an exploration recommended.

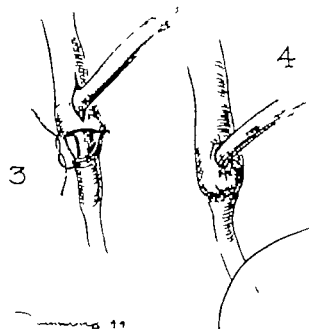
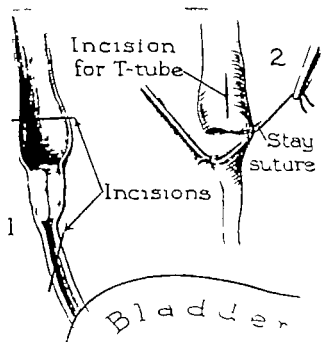


Fig. 1. Diagrammatic representation of ureter in section, showing growth and its lumen. Lincs show areas where ureter was cut off. 2 Stay sutures draw cut ends and ureter together and slit was made above to insert T tube.

Fig. 3 and 4. Cut ends of ureter being approximated around T-tube with lower arm of T tube extending into the lower ureter. Continuous suture of No. 0000 catgut was used after stay sutures were tied.

An incision 10 inches in length was made in the lower right quadrant of the abdomen lateral to the rectus muscles, with the anterior superior spine in the middle of it, but 2 inches medial to it. The external oblique muscle was split in the direction of its fibers, while the internal oblique and transversalis muscles were cut and the ureter was exposed by pushing the peritoneum toward the midline. Just below the brim of the true pelvis the ureter showed a hard area which was discrete and not attached to any surrounding structures. The ureter immediately above the lump was quite dilated while the ureter below was not enlarged but the usual size. No evidence of any secondary tumors was seen. It was believed that this was a new growth, primary in the ureter and the decision was made to excise it and join the 2 ends. The ureter was freed well up to and including the kink and plenty of slack ureter was present. Figure 1 (1) shows where the ureter was cut across in relationship to the growth. The upper portion was cut straight across and the lower portion cut on a slant. This was done in order to make the lower small ureter approximate more closely the size of the upper ureter. Figure 1 (2)—A slit was made in the upper portion and a stay suture introduced to hold the edges together. In Figure 3 the small T tube has been inserted and the lower end carried into the lower ureter. Several stay sutures were inserted after which a continuous suture was placed around the area of the anastomosis. When this portion of the operation was finished, it was believed that this should give a water tight joint. No tension was present, but the ureter was quite slack. No 0000 plain catgut was used to suture the

ureter. The wound was closed in layers a small tube being left down to the site of the anastomosis.

The wound was quite dry until the sixteenth day when urine began to come around the tube and the patient had a low fever. This continued until his twenty first day when the T tube was withdrawn. The wound was wet a few hours only and completely dry in twenty four hours and did not leak again.

The urine in the meantime had begun to show a good deal of pus. The prostatic secretion also contained a good deal of pus. A few prostatic massages and mandelic acid cleared the urine, the temperature came down and the patient's condition was much improved.

Twenty six days after the operation an attempt was made to catheterize the right ureter. Various catheters were used these were blocked immediately at the ureteral orifice and did not reach the site of the anastomosis. It was decided that edema was causing the obstruction and an attempt should be made at a later date to dilate the ureter.

Three and one half months after the operation under spinal anesthesia the McCarthy panendoscope was used, and a large No. 12 bougie passed up the right ureter. This was obstructed at 5 cm. but went through with a little difficulty. It was withdrawn and a No. 11 Garceau catheter was passed. Good dilatation was obtained. Six weeks later dilatation was repeated under local anesthesia. Some slight obstruction was present but the ureter was dilated easily.

The pathological report was papillary carcinoma
JOSEPH K. NARAT M.D.

Roberts, M: An Analysis of 90 Cases of Transplantation of the Ureters for Obstetric Vesicovaginal Fistula. *J. Obst. Gyn. Brit. Empire*, 1944, 51: 519.

A series of 90 patients with obstetric vesicovaginal fistula treated by transplantation of the ureters into the colon is presented. Various techniques were used, and the operative results are tabulated. The mortality with each technique may be seen from the following table

TABLE I—RESULTS OF 2 DIFFERENT METHODS (OMITTING 2 ANESTHETIC DEATHS)

Type of Operation	Cases	Deaths	Mortality per cent
A. Winsbury-White	9	3	5.8
B. Coffey No. 1—two-stage	41	—	3.4
C. Coffey No. 2—two-stage	7	5	30.7
D. Coffey No. 3—two-stage	3	—	—
E. Coffey No. 4—two-stage	5	—	50.0
F. Mixed, in two stages	4	1	5.0
G. Mixed in one stage	3	—	—
Average mortality 12.			
All types in one stage	24	6	5.0
All types in two stages	66	5	7.8

The author does not compare these techniques with repair of the fistulas, nor does he evaluate the more remote results. JAMES F. DONNELLY, M.D.

BLADDER, URETHRA, AND PENIS

Bellie, C. J.: Cystostomy after Spinal Anesthesia. *Surgery* 1944, 16: 896.

Ninety-four men without urological diseases and with ages ranging from eighteen to thirty five were operated on under spinal anesthesia, and cystostomies were made as soon as sensation below the level of anesthesia returned. The procedure followed in this investigation was detailed and an illustration thereof was published in the article.

Controlled determinations were made on 5 persons who had been given intravenous sodium-pentothal anesthesia for very short operations. The results showed that in the spinal-anesthesia group the intra-vesical tension increased slowly as the bladder was distended with fluid. The strong rhythmic contractions indicated by fluctuations in the manometer column coincident with the desire to void, occurred at greater volumes and at higher pressures than in the controls.

Since the stretch reflex for the bladder is in the sacral cord, it is not surprising that residual vesical effects are found after the use of spinal anesthesia.

A discussion of the results obtained included the anatomy of the nervous supply to the bladder in relation to micturition. Spinal anesthesia is considered to establish temporarily a type of neurogenic vesical dysfunction probably due to the anesthetic agent. The bladder wall remains somewhat insensitive to its distending contents, and although the expulsive force of the detrusor muscle may actually not be diminished, the normal strong reflex vesical

contractions which coincide with the desire to void do not appear until the volume of the bladder and intravesical tension are so great as to invite further pressure anesthesia of the wall and a continued sensory type of retention which initiates urinary infection.

An early catheterization by preventing pressure anesthesia of the bladder wall, will facilitate early subsequent spontaneous voiding while delayed and widely spaced catheterization serves to aggravate the neurogenic dysfunction and precipitate infection.

MARY KARP, M.D.

Emmett, J. L., and Cristol, D. S.: Urinary Retention Following Surgical Operation on the Rectum and Sigmoid. *J. Am. Med. Ass.*, 1944, 36: 1077.

Urinary retention in the male patient after operations on the rectum and sigmoid is not as complex as has been heretofore supposed. Reduced to its basic components it may be stated simply. Most patients subjected to this type of operation are in the age of prostatic. It has been recognized for years that many factors such as chilling, alcoholic or sexual excess overeating or surgical operations on other parts of the body will precipitate urinary retention in such cases. Trauma to the prostate and urethra plus the removal of the supporting structures around the base of the bladder (such as occurs after posterior resection or combined abdominoperineal resection) furnishes an ideal situation for the bladder to decompensate and become unable to expel urine through a moderately obstructed vesical neck.

Instead of an attempt to increase the vesical tone (which is impossible by any means available at present) the rational procedure is to weaken the vesical neck and obviate the imbalance that exists between the detrusor muscle and the vesical neck. This can be easily accomplished by transurethral prostatic resection and will completely and quickly relieve nearly all patients suffering from this annoying condition. To avoid an unnecessary operation it is probably best to allow the patient a period of at least three weeks after the intestinal operation to regain his vesical function before transurethral resection is advised.

Berry, H. C.: Traumatic Rupture of the Urethra and Bladder. *Austral. N. Zealand J. Surg.* 1944, 14: 104.

Rupture of the lower portion of the urinary tract, although relatively rare, is, nonetheless, important because early adequate treatment may avert a serious or undesirable outcome. Traumatic lesions of the lower urinary tract may be classified into three main groups: namely, (1) ruptures of the anterior urethra, complete or incomplete; (2) rupture of the posterior urethra, complete or incomplete; and (3) rupture of the bladder extraperitoneal or intraperitoneal. The anterior urethra is ruptured by direct violence, and usually it is the bulb which is crushed against the pubic arch. The lesion is often diffuse and the periurethral tissues are pulped. Rupture of

the posterior urethra is associated with a fractured pelvis and is caused by indirect violence. The lesion is more circumscribed, but there is often wide separation. Traumatic rupture of the bladder is usually a complication of a fractured pelvis but it may follow direct trauma to a distended bladder. Although penetrating injuries due to missiles of war will not fit into this classification, the principles of diagnosis and treatment are similar.

Rupture of the anterior urethra commonly follows a fall astride or a blow to the perineum in the male. The presenting signs are bleeding from the meatus, bruising in the perineum, and retention of urine. Shock is seldom severe. Catheterization is unnecessary for diagnosis. In typical cases the spasm of the sphincter prevents extravasation of urine for several hours. Unless the injury is at the distal end of the penis and the patient is able to void satisfactorily early suprapubic cystostomy is indicated. In many cases this is all that is necessary but when perineal hematoma is present or in late cases with extravasation of urine, perineal drainage must be established. Perineal incision also permits of inspection of the urethra and suture of the divided ends. If the tissues are edematous and the urethra cannot be united without tension, only the roof of the urethra should be sutured. Early suture is not essential provided diversion of the urine is adequate. Suprapubic drainage must be maintained until the perineum is healed and any stricture is fully dilated. An indwelling urethral catheter except when the edema has subsided and the wound is healing is contraindicated by the danger of infection and increasing stricture formation. Regular dilatation of the urethra following healing of the wound must be carried out in some cases for a few months, and in others for life. Complications depend on the residual urethral stricture and its sequelae perineal abscess, urinary fistulas, urinary infection and calculus formation, chordee, sterility and impotence.

Rupture of the lower urinary tract occurs as a complication of a fractured pelvis in probably less than 5 per cent of cases. It depends upon the site of fracture and the degree of displacement of fragments. Rupture of the lower urinary tract must always be suspected when separation of the symphysis or fracture of the pubic ramus is present and especially in cases of complete fracture dislocation of the pelvic girdle. The urethra may be torn where it is held fixed by the membranous sphincter and either the bladder or urethra may be pierced by sharp fragments of bone. When the pelvis is laterally compressed and its anteroposterior diameter increased the puboprostatic ligaments may be torn and as blood and urine accumulate in the prevesical space the bladder and prostate may be rotated upward and backward until there is often a gap of an inch or more between the torn ends of the urethra. In neglected cases the bladder may become anchored in its new position and late attempts at restoration may be fruitless. In these types of rupture the injury is often rapidly fatal or the patient is in such severe

shock that restorative measures must be instituted immediately to preserve life. Reduction of the displaced fragments of the fractured pelvis prevents further shock and hemorrhage and may bring together the torn ends of the urethra. Temporary immobilization of the pelvis by a pelvic sling until operative measures to drain the bladder and restore the urethra are instituted is indicated. Diagnosis of intrapelvic rupture is established by the presence of suprapubic tenderness and dullness, retention of urine, bleeding from the meatus and dislocation of the prostate upward. At this stage intrapelvic rupture of the urethra and extraperitoneal rupture of the bladder can rarely be distinguished. When there is doubt expectant treatment should never be adopted. A catheter must be passed and only if a normal amount of clear bloodless urine is withdrawn can the urethra and bladder be considered intact. When bloody urine is obtained the catheter may lie in the prevesical space or in the peritoneal cavity and suprapubic cystostomy and exploration are indicated. Accessory investigations such as retrograde and excretion cystograms and injection and withdrawal of known quantities of solution are uncertain and unnecessary and they waste time. At the time of suprapubic cystostomy a urethral catheter is passed retrogradely. If it passes into the bladder it is removed a suprapubic catheter is left in the bladder and the prevesical space is drained. When the membranous urethra is completely torn the catheter will pass into the prevesical space. A sound may be introduced into the bladder by manipulation and an indwelling catheter splinting the urethra is withdrawn. If there is a tendency for the displacement of the bladder to persist, traction on a Foley type of catheter may be used to exert a constant pull on the bladder neck. Here also an indwelling splinting catheter is undesirable but the soft parts must be kept in position at all cost. Direct suture of the membranous urethra, although theoretically the most desirable treatment, is attended by an increased risk to an already shocked patient. Late attempts at restoration of inadequately treated ruptured membranous urethras usually are unsuccessful and incontinence is usual.

Rupture of the bladder occurs as a complication of a fractured pelvis or following direct trauma to a distended bladder. About two-thirds of the ruptures are intraperitoneal and the mortality in these cases is about 50 per cent, depending also upon the severity of the concomitant injuries and the time elapsed between rupture and drainage of the bladder. In gunshot wounds, especially of the buttocks, in fractures of the pelvis, or when there has been a blow to the abdomen (especially in an alcoholic) the possibility of rupture of the bladder must be investigated by catheterization. If clear bloodless urine is not obtained the patient must be operated upon immediately. A suprapubic incision having been made an extraperitoneal rupture is obvious by the wide spread extravasation of blood and urine. Cystostomy is performed and the bladder is explored to exclude

any intraperitoneal lesion. If there is doubt the peritoneum may be opened and closed immediately if no free fluid is present. The prevesical space should be drained. If there is no extraperitoneal rupture the peritoneum is opened, the anterior wall of the bladder is opened extraperitoneally for drainage and the rent in the bladder is repaired. The peritoneal cavity is drained for twenty four hours, the prevesical space a little longer and the cystostomy is maintained for two weeks. In gunshot wounds, injury to other viscera must be excluded. WILLIAM W. SCOTT M.D.

Taylor J. A.: Penile Horn. *J. Urol. Balt.*, 1944, 53, 6.

Cutaneous horn, according to Ewing, is a peculiar form of cutaneous wart marked by excessive and progressive keratosis. These horns may appear anywhere on the skin of the body and are infrequently found on the penis. When found on the penis they are usually on the glans and may be single or multiple.

In view of the fact that these horns grow on a wart or acanthoma and are merely a progression of the keratosis already present in these two conditions, then it would seem that they are the result of prolonged irritation usually from a long prepuce.

Keratosis is a general term applied to pathological epidermoid proliferations, and the importance of keratosis as a precursor of cancer cannot be overestimated.

The author's patient was a thirty-five-year-old German male. His mother and father had both died of cancer. There was no relevant past history. His present illness began in Germany three years before when he noticed a small wart on the left aspect of his glans penis. The prepuce was adherent to the glans so a circumcision was performed, and the wart was excised. It recurred promptly and grew until it was again removed in March, 1939 in this country. On admission it had recurred and the patient presented a warty growth 1 cm. in diameter on the distal lateral aspect of the glans penis. General physical examination was essentially negative.



Fig. Firm, hornlike growth from the penis.

Under low spinal anesthesia, the warty growth was excised with the electrosurgical knife. The pathological report read as follows: Macroscopically the specimen consists of a wedge-shaped piece of tissue 12 mm. long which has the appearance of a verruca. Microscopically, sections through the tissue show the growth to be composed of broad papillary masses of squamous epithelium with a few pearls but consisting largely of prickly cells. The basal layer is hypertrophic, and there are many mitotic figures. The tumor is growing in a papillary manner but with long extension of cells into a very vascular stroma. The type of cells and the manner of growth are more extensive than occurs in a papilloma and the growth should be considered an epithelioma, but being highly differentiated and not showing deep infiltration with single cells, it is a Group I.

The patient was readmitted to the hospital in October 1940 eleven months later with a recurrence of verrucous growths extending to the coronal sulcus. Under low spinal anesthesia the growths were widely excised with the electrosurgical knife. This time examination of the specimen macroscopically showed a tumor of the penis in several portions, the largest 1 1/2 by 8/10 cm. in size.

The patient was readmitted to the hospital in July 1943 saying that several weeks after discharge, a small wart appeared and that one month later a horn began to grow out from this wart. It had grown steadily and at present was slightly over 3 inches in length. Under low spinal anesthesia the horn was removed with the electrosurgical knife, a deep wedge being cut into the glans.

The specimen consisted of a firm hornlike growth from the penis 9 cm. long by 3 by 2 cm. at the base and 1 cm. thick at the rounded tip (Fig. 1). On section the base showed papillary outgrowth from the underlying derma. The line of the base was even and there did not appear to be any outgrowth. There was an additional portion from the base of the growth. On section it showed epithelium from 4 to 7 mm. thick with vertical striation on one surface, and beneath this, a fibrous base. Microscopic sections through the base of the growth showed it to be composed of very long strands of hypertrophic squamous epithelium with many anaplastic changes and pearl formation in the deepest portion.

JOHN A. LOER M.D.

GENITAL ORGANS

Bumpus, H. C., Jr. Massey B. D., and Nation. E. F.: Experience with Orchiectomy for Carcinoma of the Prostate. *J. Am. Med. Ass.* 1945, 27, 67.

The results obtained with bilateral orchiectomy in 25 patients with carcinoma of the prostate are here reported. All of these persons, with 1 exception, showed decided improvement following the operation. Such improvement included such changes as increased vigor, strength, weight, and appetite, a

sense of well being, cessation of pain, and diminished urinary difficulties.

The majority of these patients, although not all of them, were given diethylstilbestrol in doses ranging from 1 to 3 mgm. daily following orchectomy, and 13 had a transurethral prostatic resection in addition to the castration. The condition of the patient which was not improved remained about the same for six weeks before it began to grow worse; however the patient was still alive thirteen months after the orchectomy the metastases progressing and his health failing. (No case histories are appended.)

In the discussion of the results, all of these cases are divided into three groups: (1) 4 patients operated upon two years ago or more; (2) 11 patients operated upon between one and two years ago; and (3) 10 patients operated upon within the past year. Three of the first group cited are alive and well—1 patient at thirty months after orchectomy. One of the 3 had extensive pulmonary metastases which receded after the operation. The fourth is failing rapidly twenty-nine months after operation. Of the second group, 5 are dead, 4 are well, and 1 had a relapse after twelve months of relief. All of the patients in the third group are free of symptoms which indicate advancing malignancy.

There was considerable variation in the length of time required for softening of the prostate after orchectomy and the administration of diethylstilbestrol. There seemed to be no correlation between the length of the interval and the grade of malignancy.

In concluding the authors stress the fact that since 40 per cent of their patients who have been observed for a year or more following orchectomy have had a recurrence of symptoms it is anticipated that all will eventually have a relapse. It remains therefore, to regulate better our use of orchectomy or of the estrogens. It should be delayed probably until symptoms of an advanced malignant condition are manifest, then either method should be used separately or in succession rather than simultaneously.

The authors desire to call particular attention to a remarkable transformation in the patient's state of mind and personal habits (from a slovenly apathetic habitus, to that of neatness, alertness, and interest in his surroundings) which occurred in a striking manner in one of these individuals, and which was more or less manifested by all the patients, immediately following the operation of bilateral orchectomy. This personality transformation is believed not to have been reported previously in the medical literature.

JOHN W. BRENNAN, M.D.

Emmett, J. L. and Greene, L. F.: Bilateral Orchectomy for Carcinoma of the Prostate Gland. *J. Am. Med. Ass.*, 1945, 127, 63.

The indication for bilateral orchectomy is carcinoma of the prostate with metastasis. Bilateral orchectomy is especially efficacious when the metastatic growths have given rise to symptoms. The

period of relief following orchectomy varies from months to years, but whether any patients will remain permanently relieved seems extremely doubtful. Apparently the large majority of patients have a recurrence of symptoms within a year. Whether or not "prophylactic" orchectomy (done in the early stages of the disease before metastasis has appeared) measurably influences the course of the disease is not yet known. This problem cannot be settled until more time has elapsed and a larger series of cases in which prophylactic orchectomy has been performed has been studied. Until this problem has been definitely settled the present practice of the authors is to advise orchectomy primarily for patients suffering from metastasis for the relief of metastatic symptoms. Results to date suggest that when orchectomy is performed in conjunction with transurethral resection the frequency of recurrent obstructive symptoms requiring subsequent prostatic resection is reduced; furthermore, if such symptoms do appear the time interval between resections is increased.

The authors are also treating a group of patients who do not show evidence of metastasis with estrogens after transurethral resection to see if the course of the disease can be appreciably altered over a substantial period. They are interested to know if preliminary estrogenic therapy in such cases will tend to nullify the palliative effects of castration if the latter should become necessary for the control of symptoms later on.

Neesbit, R. M., Pazzos, R., and Cummings, R. H.: The Treatment of Prostatic Carcinoma by Castration and by the Administration of Estrogenic Hormone. *J. Urol.*, Balt. 1944, 52, 570.

The authors compare the results of castration in a series of 75 cases of prostatic cancer from six months to two years after operation with the results in a parallel series of 50 cases treated by the administration of 1 mgm. of diethylstilbestrol daily over periods of from six to thirty-five months.

In both series the relief of pain and the increase in weight have been striking. Complete relief of pain resulted in 64 per cent of the cases subjected to orchectomy as opposed to 56 per cent of the stilbestrol treated cases. Weight gain was better in the stilbestrol series (78 per cent and 72 per cent respectively). Relief of partial urinary obstruction was greater in the orchectomy cases (86 per cent compared with 65 per cent). This would suggest that regression of the carcinoma was more complete following orchectomy. Following orchectomy 85 per cent of the carcinomas decreased in size and 15 per cent became softer as judged by rectal examination. The comparable results with stilbestrol were decrease in size in 33 per cent and softening in 16 per cent. In no castration case was the lesion observed to enlarge or fail to change in consistency or size, whereas in the stilbestrol series increase in size occurred in 12 per cent and no change was observed in 39 per cent of the cases. Metastases

regressed in 33 per cent of the castration cases, whereas in no case given stilbestrol did the metastases regress. Increase in the number and size of the metastases occurred in 67 per cent of the castrated patients and in only 38 per cent of those receiving estrogen. Deaths in the castration series amounted to 7 per cent, and in the estrogen series, to 8 per cent. Favorable responses occurred in 73 per cent and 80 per cent, respectively and whereas there were no immediate failures in the stilbestrol group 7 per cent of the castrated patients failed to derive any immediate benefit from the operation.

One case is presented in which the serum acid phosphatase failed to increase coincidentally with roentgenographical and clinical progression of the disease. Histopathological examination in this case revealed an abundance of acid phosphatase in the metastases.

The authors conclude that the acid-phosphatase level of the serum is an unreliable index of metastatic carcinogenic activity. In summary they advise that although there is little difference in subjective response to the two forms of treatment, orchectomy results in greater objective regression in the primary tumor and metastases. Neither form of treatment affords prophylaxis against the development of or increase in metastases. Pain in postcastration cases can often be relieved by estrogen administration.

DONALD F. McDONALD, M.D.

Barringer B. S. The Prognosis in Teratoma Testis. *J. Urol.*, Balt., 1944, 51: 578.

The vast amount of clinical and pathological material available to the author for study in the past twenty-eight years at the Memorial Hospital, New York City is the basis for the present report.

The preoperative diagnosis of testis tumor with the exception of those rare choriomas which produce high titers of urinary gonadotropins, is uncertain. The prognosis is not altered by preoperative irradiation of the testis. A review of 69 living patients showed that 80 per cent of the tumors were seminomas and 17 per cent were adenocarcinomas. There was 1 case of spindle-cell sarcoma and 1 of adult cystic teratoma. There were no cases of chorioma.

In the case of a patient with a testicular tumor there is a large chance that he has a seminoma and a slight chance that he has an adenocarcinoma. There is only a remote chance that he has a chorioma or a nonmalignant tumor. Of 55 patients with seminoma, 56 per cent were well for five years or more but of these, 29 per cent had metastases. In the group with adenocarcinoma, 83 per cent were well as long as five years, 40 per cent with metastases. While the testicular seminoma is much more radiosensitive than the adenocarcinoma, surprisingly few patients with metastasizing seminoma survive five years, while a relatively high percentage of patients with metastasizing adenocarcinoma survive more than five years.

The lymphatics of the spermatic cord are rarely invaded by testicular tumor although metastases to

the lymph nodes pass through them. The prognosis is grave if metastases can be demonstrated in the cord, the supraclavicular nodes, the abdomen, the lungs, or the periprostatic lymphatics.

Autopsy material in 37 cases showed regional node involvement as follows: Inguinal, 10.8 per cent; pelvic and iliac, 37.0 per cent; lumbar 54 per cent; celiac, 56.8 per cent; mesenteric, 18.9 per cent; mediastinal, 48.7 per cent; bronchial, 35 per cent; and cervical 35.3 per cent. Metastasis to the inguinal nodes is rare unless the tumor perforates the tunica or capsule of the testis. In many cases the center of the metastatic nodules or nodes were broken down and hemorrhagic, and in 5 cases there was hemoperitoneum. Intracranial metastases occurred in 16.3 per cent of the cases, but examinations of the brain were made in less than half of the cases on which autopsies were made. Pulmonary involvement was present in 78.3 per cent of the cases, and 55 per cent of these had also mediastinal node involvement; the pleura was involved in 37.0 per cent of the cases. In 75.8 per cent of the patients with pulmonary involvement, the liver too was involved. The involvement of the liver being hematogenous, is unrelated to that of the testis. The spleen, diaphragm, pancreas, kidneys, adrenal glands, gastrointestinal tract, and skeleton were less frequently involved. Retroperitoneal involvement was found in 58.8 per cent of the cases, and in 33.5 per cent of these the condition was bilateral.

In conclusion, the author advises concentration on the seminoma and the adenocarcinoma. Irradiation should be bilateral because the condition is bilateral in 78 per cent of the cases. Lung metastasis has a poor prognosis because liver involvement is present in 75 per cent of the cases. More extensive resection of the spermatic cord is advocated. The Chevrassu-Hilman operation yields poor results in malignancy of the testis, which condition should be treated by orchectomy and irradiation.

DONALD F. McDONALD, M.D.

MISCELLANEOUS

Kashin, J. G. and Pinck, B. D.: Factors in Male Sterility. A Critical Review of 135 Cases. *Am. J. Surg.* 1944, 66: 346.

The present study was directed primarily to cases of male infertility not associated with obvious abnormalities such as hypospadias, cryptorchidism, and abnormal attachment of the epididymis to the testis. This study included a careful medical history with emphasis upon endocrinological and sexual factors, physical examination, and, when necessary, cystoscopy and catheterization of the ejaculatory ducts. Laboratory and x-ray examinations were made as indicated. At least two semen specimens were obtained by withdrawal and ejaculation into a glass container after five days abstinence, and examined within an hour or two for motility, volume, count, mucolysis, and differential morphology. The criteria of morphology were those of Pollak and Joel,

and the motility was expressed in per cent as the ratio to nonmotile forms which lie in one-quarter of the microscopic field through an Ehrlich ocular screen. The total sperm count was determined in the counting chamber with 4 per cent boric acid, and 1 per cent phenol as a diluent. A histological study of a seminal smear stained with Macheal tetrachrome stain was made. The normal values were motility 80 per cent after two hours, sperm count, from 60 to 150 million per cubic centimeter, and morphology less than 30 per cent of abnormal forms.

A detailed analysis of 135 consecutive cases of sterile marriages indicated that the greatest correlation existed between a decreased sperm count and an increased per cent of abnormal forms and infertility. Motility and viability did not appear important. In only 31 per cent of the 135 sterile marriages were the semen analyses normal. In 25 per cent of the cases there was a decreased sperm count, an increased number of abnormal spermatozoa, and usually a decreased motility. The authors believe it is in this group of cases that endocrinological factors are responsible for sterility and that testicular biopsy should be performed. In 25 per cent of the cases a normal sperm count was associated with a high percentage of abnormal forms, and it is in this group that the casual observer may pronounce a semen specimen normal unless special morphological studies are performed routinely. The etiology in this group is often obscure, but endocrine deficiency foci in infection, exposure to x rays, or dietary deficiency must be considered. Semen analyses by 2 recent gonologists showed normal counts and motility but there was a shift to the immature types of spermatozoa among the abnormal forms present—probably the result of stimulation of spermatogenesis. Aspermia was present in 24 (18 per cent) of the 135 cases. Among these 24, 10 patients had obstruction of the genital pathways due to past epididymitis, and 14 had defective spermatogenesis. Of those with defective spermatogenesis 3 had had mumps orchitis, 1 had a history of seminoma with x ray therapy and 3 were found to have endocrine dysfunction. In only 1 case was improvement noted upon treatment with thyroid, corticosterone and gonadotropins after two years of therapy. Impregnation was successful.

Treatment in cases of definite endocrine deficiency often was attended by dramatic results. However these cases were few. When hypothyroidism was present, thyroid medication gave good results. Gonadotropins were ineffective. Vitamin B₁, B complex, and vitamin E were given in large doses, alone and with gonadotropins but with no effect. Treatment of foci of infection was followed in some cases by improvement in the semen. In cases with excessive numbers of spermatozoa and an inordinate number of abnormal forms of the immature type, testosterone propionate (10 mgm. twice a week) caused a decrease in the total number and percentage of abnormal spermatozoa. Epididymovasectomy in cases of obstructive aspermia was unsuccessful. The

authors comment that their results in five years in 135 cases are discouraging as pregnancy resulted in only 11 per cent of the entire series.

The authors conclude that endocrine therapy plays a limited role in most cases of male sterility.

DONALD F. McDONALD, M.D.

Usher G. S., and Cowan H.: Venereal Diseases Among the Migrant Farm Laborers of New Jersey. *J. M. Soc. N. Jersey* 1945 42 11

1 Of about 2,800 migrant farm workers in the potato-growing section of New Jersey 756 were examined for venereal diseases. The examinations included blood tests and inspection for lesions and for gonorrhea. The women received routine gonococcus cultures.

2 The venereal disease rate was found to be very high especially in women from fifteen to twenty four years of age. In the latter group 63 per cent of those examined were found to have darkfield positive lesions of early syphilis and 30.6 per cent were found to have gonorrhea.

3 Most of these infections were "imported to New Jersey. The hazard to the areas through which these people travel and to the people of New Jersey is pointed out.

4. The living conditions of these workers are favorable to the spread of the diseases. These conditions urgently need correction.

5 Routine medical examination of all migrant workers and prompt application of rapid treatment methods are needed. Legislation to require such examinations and perhaps enforcement of the Interstate Quarantine Law would be helpful.

JOHN A. LOFF, M.D.

Exley M.: Penicillin Treatment of Sulfonamide-Resistant Gonorrhea with Results of Multiple and Single Injection Methods. *J. Urol., Balt.*, 1944, 52 626

Two hundred and fifty-one cases of sulfonamide-resistant gonorrhea were treated with varying amounts of penicillin.

The dosage varying from 41,300 to 125,000 Oxford units was administered by intramuscular injections.

The result of the asymptomatic cure by means of the single injection treatment is dramatic. The amount of penicillin used should be at least 80,000 Oxford units. The absorption-elimination time is short, and this method may later be found to be more efficacious in previously untreated gonorrheal urethritis.

Excess dilution is frowned upon for the intramuscular treatment. This not only causes needless pain at the site of the injection but also a more rapid rate of absorption. In another series being treated at present and to be published later this has been found to be true.

There were only 3 cases with toxic manifestations in this series all were transient and minimal in nature.

The follow up examinations on the armed-service cases comprising 77 per cent of this series, have all been negative by culture and smear. The follow-up of the merchant service has not been as satisfactory, but the total average time of examination in both groups was thirty-one and two-tenth days. An average of 2.8 examinations have been made after the discharge of the patient from the hospital.

The average time for the cultures to become negative in all groups was twenty-one and one-tenth hours. The change may have occurred earlier but it was inexpedient to make tests at more frequent intervals.

Although the number of cases in this series is small the use of penicillin is a gratifying addition to the curative armamentarium in the treatment of epididymitis associated with gonorrheal urethritis.

The combined use of hyperpyrexia and chemotherapy has yielded satisfactory results. There are still cases of failure in which this type of treatment will have to be utilized. The hospitalization time has been drastically reduced by the advent and substitution of penicillin.

An evaluation of the treatment from the results obtained leads the authors to believe that certain methods used in this series are the most satisfactory. They are inclined toward the multiple-injection treatment, their preference being either 2 injections of 50,000 Oxford units for a total of 100,000 Oxford units, or 5 injections for a total of 80,000 Oxford units. At the present time they are running a larger series of the latter group.

The total treatment period has been reduced to below nine hours by means of the multiple injection method.

The total dosage of penicillin has been reduced

From the observations made it does not seem desirable nor expedient, at this time to recommend

the one-day ambulatory treatment until further clinical studies have been made.

JOHN A. LOAR M.D.

Bowworth, N. L., Riba, L. W., and Schmicklapp, C. J.: Two Hundred and Thirty Three Cases of Sulfis Resistant Gonorrhea Treated with 50,000 Units of Penicillin. *J. U. & Balt.* 1944, 51: 631.

Fifty thousand units of penicillin is an insufficient dosage to clear the average male gonorrheal infection—the results are failures in 23 per cent of the cases treated by this dosage.

A high incidence of positive and doubtful smears occurs during the first fourteen post treatment days, but this indicates neither penicillin success nor failure. Positive smears and cultures usually indicate failure of cure.

Treatment with 100,000 units will clear the majority (85 per cent) of the 50,000-unit failures.

Hyperpyrexia and 100,000 intravenous units of penicillin will clear 30 per cent of the apparent penicillin-resistant gonorrheal infections. With an increase of penicillin supply larger doses may be indicated during fever treatment.

Gonococcus carriers may also be produced with penicillin therapy particularly when insufficient dosages are given.

One hundred and sixty thousand units of penicillin administered intramuscularly will result in the highest percentage (93 per cent) of clinical cures in the present-day treatment of sulfonamide-resistant gonorrheal infections.

Patients with complications should have correspondingly larger doses.

Penicillin is an excellent gonococcal bacteriostatic. The clinical cure occurs as a result of the host's defense mechanism provided it is not disturbed by too much interference. JOHN A. LOAR M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Boger W P: Pneumococcic Arthritis. Report of a Case of So-Called Primary Pneumococcic Arthritis. *J Am. M. Ass.* 1944; 126 1063

Pneumococcic arthritis should be regarded as the result of a septicemia.

A case of pneumococcic arthritis is presented in which no infection other than that in the knee could be demonstrated. A negro woman aged fifty was seized with sudden acute pain in the left knee. The next day the knee was swollen and painful on motion. During the following days the knee became more swollen and painful and the patient had a fever.

The patient was admitted to the hospital on the tenth day. The history showed no evidence of any previous infection. The temperature was 103 F the pulse rate 100, and respiration 25. The blood pressure was 125/85. The left leg was swollen from the hip to the ankle and was easily twice the size of the right leg. This increase in size of the leg was due primarily to a pitting edema limited to the dependent aspect of the leg from the left hip to the ankle. Large engorged veins were present over the patellar and lateral aspects of the knee and other signs of inflammation were present. There was effusion of the knee joint, the patella was ballotable, and the knee joint was very tender and hot to touch. Movement of the joint was painful and limited. Fluctuation was present. No lymphadenopathy was present in the left groin.

A diagnosis of acute septic arthritis was made. The first aspiration produced 310 cc. of thick yellowish-green pus from the knee joint, and examination revealed type XII pneumococcus in pure culture.

Sulfadiazine was given in full dosage. The patient's temperature subsided on the fifth day and was only slightly elevated after that. A second aspiration produced 340 cc. of pus. Five grams of sodium sulfadiazine dissolved in 100 cc. of distilled water was then injected into the joint. Aspiration was repeated on the sixteenth, nineteenth, and twentieth days but no organisms were found in the pus.

X-ray films did not reveal any bone destruction in the knee joint. The hemoglobin averaged 58 per cent and the red count averaged 3,410,000. One transfusion was given. The high white-cell count was 12,300 and all other counts averaged 7,460. The differential counts did not show more than 76 per cent polymorphonuclear leucocytes. Six blood cultures failed to yield a growth.

The patient was discharged on the thirty-second day with a painless knee joint and was able to walk without discomfort. The range of motion was 90 degrees.

The listed cases of pneumococcic arthritis are given. The classification of the symptoms, clinical

features, bacteriology, pathology treatment, and prognosis are discussed in detail.

RICHARD J BENNETT JR., M.D.

Boger W P: Purulent Meningococcal Arthritis. *Am. J. M. Sc.* 1944 308 708

Two proved cases of purulent meningococcal arthritis are presented and it is suggested that the prognosis in joint manifestations of meningococcal infections is not so uniformly favorable as is usually stated in the literature.

CASE 1: A fifty-two-year-old white widow entered the hospital with a temperature of 103 F. She complained of pain in every joint. Several weeks previous to entry the patient had been complaining of vague, coldlike symptoms with general muscular aching and nausea. Physical examination after hospital admittance disclosed a fine purpuric rash over the ankles and lower thirds of both legs, and in addition, several petechiae on the thighs and abdomen. Scattered over both hands, forearms, and feet were several larger purpuric spots which measured from 3 to 10 mm. in diameter. Resemblance was noted to erythema nodosum and to Haverhill fever. The general picture exhibited redness and swelling of spots redness and exquisite tenderness over both elbow joints, both ankle and wrist joints, and swelling of the hands and feet. There was a splotch of purple discoloration over each of the metacarpophalangeal joints and the dull red of inflammation about both wrists.

Aspiration of the left knee was done and approximately 50 cc. of thick, yellow pus was obtained. On smear countless numbers of both intracellular and extracellular gram negative diplococci were found. Later both the blood culture and the culture made from the joint fluid were reported as showing growths of meningococci. The organism was typed as a type I meningococcus by the National Institute of Health.

After nineteen days of therapy with sulfadiazine the white count was 3,200 the patient was running a mild fever and most of the joints had become painless, but the left knee was still swollen, and the right hand was still definitely swollen. The knee could be flexed beyond 90 degrees but it felt stiff. Grasping with the right hand was poor and the wrist could not be dorsiflexed.

The follow up of this patient revealed that on the eighteenth day from the onset of her arthritis the left knee still ached, the left ankle swelled after walking, and the right hand remained swollen. A roentgenogram of the right wrist revealed destruction and narrowing of the joint space due to infectious arthritis.

CASE 2: A white, single woman twenty four years of age, had been employed in social work for several months and had been visiting in numerous homes.

She was taken with a cold, headache, muscle soreness, and a rash. Examination revealed a temperature of 102° F., slight soreness of the muscles generally, mild headache and some nausea. The neck was slightly painful on anterior flexion. The skin presented a hemorrhagic rash limited to the arms and legs, and both palms and soles presented spots ranging from 5 to 10 mm. in diameter. A lumbar puncture was done and slightly cloudy fluid was obtained. This revealed 500 cells per cubic millimeter. Organisms were not seen on smear but culture of the fluid was positive for meningococci. A blood culture taken at this time was noted to be positive for meningococci. The left knee was somewhat swollen but the patient herself had not been aware of this fact. There was no pain on manipulation of the joint, but flexion was a trifle limited by a feeling of "fullness." There was no redness or tenderness. Aspiration was done and a thick, yellowish fluid was obtained which, on smear, revealed gram-negative diplococci. Culture of this fluid was positive for meningococci. The patient recovered without later sequelae under treatment with sulfadiazine.

JOHN W. BARNES, M.D.

Shank, R. E., Glider, H., and Hoegland, C. L.: Studies on Diseases of Muscles; Progressive Muscular Dystrophy; A Clinical Review of 48 Cases. *Arch. Neur. Psychiat.*, Chic., 1944, 51: 431.

A clinical study of 40 patients with progressive muscular dystrophy gave evidence of the hereditary nature of the disease. Fourteen of the 40 patients were from families in which other cases of the disease had occurred. There were examples of dominant sex-linked and simple recessive types of inheritance. Both pseudohypertrophy and atrophy existed in the affected muscles, with pseudohypertrophy most frequent in the large bulky muscles of the younger patients.

The early onset of the disease was demonstrated, the first symptoms having been noted by 63 per cent of this series of patients before the age of ten years. When the onset was delayed until late childhood or early adult life, the first muscles involved were frequently those of the scapulohumeral group.

The course of progressive muscular dystrophy was most rapid in patients with onset of the disease before the fifth year of life.

There were characteristic changes in the roentgenograms of patients with progressive muscular dystrophy. These alterations include conspicuous streaking of the soft-tissue shadows of affected muscle, delayed appearance of centers of ossification in the bones of the hands and in the epiphyses of the long bones, and demineralization of other bony structures.

The rate of excretion of creatine was greater and the rate of excretion of creatinine was less in boys with muscular dystrophy than in normal boys of the same age group who were maintained on diets of identical composition. These differences were increased when the subjects were fasting.

The concentration of creatine in the plasma of dystrophic children was greater than the concentration in the plasma of normal subjects. Levels of creatinine in the plasma were unchanged.

The creatine tolerance of children with progressive muscular dystrophy was not significantly different from that of normal children of the same age group.

The basal metabolic rate was low in children with the disease. The median basal metabolic rate for a group of 14 patients was 14.5 per cent of the normal standards.

The fasting level of the blood sugar and the response to intravenous administration of dextrose were essentially the same in dystrophic patients as in normal subjects. One patient with muscular dystrophy gave evidence of an increased rate of utilization of dextrose injected intravenously.

Patients with progressive muscular dystrophy were in positive nitrogen and phosphorus balance.

Within recent years various types of therapy, including treatment with aminocaproic acid, vitamin E and pyridoxine, have been proposed for progressive muscular dystrophy. After thorough trial, each of these methods has proved to be singularly ineffective. Any rational approach to the successful treatment of the disease depends on more specific information concerning its nature and the metabolic changes affected by it.

ROBERT P. MONTGOMERY, M.D.

Grieve, J.: Congenital Subluxation of the Acromioclavicular Joint. *Lancet*, Lond., 1944, 247: 817.

Six cases of congenital subluxation of the acromioclavicular joint are described also a seventh milder case with gross deformity of the right acromion. The exact nature of the condition is still obscure.

Even 1 cm. of displacement of the clavicle may produce no disability. The emotional effect may be important.

ROBERT P. MONTGOMERY, M.D.

Brieda, P. C.: Tuberculosis of the Greater Trochanter and Its Bursae. *Radiology*, 1945 44: 32.

The author gives a brief review of the literature which indicates that tuberculosis of the greater trochanter and its bursa is a rare condition usually occurring secondary to tuberculous osteomyelitis of the greater trochanter. All writers agree that complete extirpation of all infected tissue, with immobilization of the affected part, followed by body-building postoperative care, is the treatment of choice.

The condition may occur in either sex and at any age although it is unusual in children. The most common complaint is mild pain in the involved leg with intervals of quiescence. Often there is a draining sinus in the region of the trochanter.

Examination shows slight swelling with tenderness to pressure but no heat or redness. There is no limitation of motion in the hip joint. Tuberculosis elsewhere in the body is quite common.

The lesion has a strong tendency to recurrence and in the later stages it extends to the neck and head of

the femur and even to the joint itself. When only the bursa is involved the percentage of cures is believed to be somewhat higher.

The first roentgen sign is a small fleck of calcium in the bursa or a minimal area of destruction in the outermost part of the trochanter which often can be demonstrated only with soft tissue exposure. Later a larger area of destruction is noted in the trochanter with osteoporosis of the adjacent bone. Sometimes an involucrum is found in the soft tissues lateral to the trochanter secondary to infection or injury to the periosteum either following operation or in draining sinuses of long duration.

The differential diagnosis includes simple nonspecific bursitis or osteomyelitis and certain osteolytic neoplasms.

The author observed 4 cases which are briefly described and illustrated with the respective roentgenograms.

T. LUCUTIA, M.D.

Keen, P.: Pellegrini-Stieda Disease in the Bantu. *Clin. Proc. Capetown*, 1944, 3: 331.

The author describes 17 cases of Pellegrini-Stieda disease in the Bantu. A total of 20 cases were observed in eighteen months.

The anatomy of the medial collateral ligament in the Bantu has been described and differences have been noted. It appears that the medial collateral ligament in the Bantu is a larger structure, the insertion of which into the condyle of the femur is intimately associated with that of the tendon of the adductor magnus. Its insertion into the tibia is similar to that of the hamstring muscles.

In addition, it was noted that there were cellular spaces around the tendon of the adductor magnus, particularly between this tendon and the vastus medialis, where a branch of the genicular artery passes forward. This space communicates with the upper insertion of the medial collateral ligament and could harbor a hematoma which might undergo ossification if osteoblasts were released by the trauma. This might explain the tendency of the ossified masses to extend upward beyond the limits of the medial collateral ligament.

In 10 of the 17 cases in this series, as judged from the roentgenological appearances the ossification had extended beyond the limits of the ligament. In 4 other cases the ossification did not appear to be in the ligament at all, and in only 3 cases did it seem to be entirely confined to the ligament. For details on the etiology Kulowski's paper should be consulted.

In the present series of Bantu cases the intimate connection with the adductor magnus tendon might account for the upward spread beyond the limits of the medial collateral tendons. This fact might also account for the frequency of this condition in the Bantu. The extra strain on the upper part of the medial collateral ligament where practically all the ossification occurs might be caused by the action of the adductor magnus which apparently has a direct connection with the medial collateral ligament in the Bantu. It is possible that the differences in anatomy

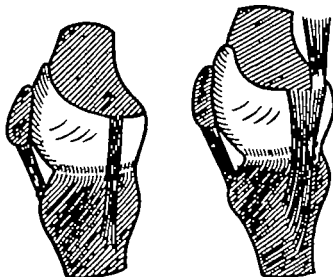


Fig. 1 Left, An average diagram.

Fig. 2 An average specimen in the Bantu.

might also account for the conspicuous absence of lesions of the internal semilunar cartilage in the Bantu.

It has been suggested that in the Bantu periosteal avulsion near the upper insertion of the medial collateral ligament is the commonest cause of this form of para-articular ossification.

The principle that the condition is a true post-traumatic lesion must be accepted on the evidence available.

In 1 case the first roentgenograph showed no abnormality but the second one, taken twenty three days later showed definite signs of ossification. With a soft ray technique the ossification would probably have been visible within eighteen days. Two other cases with negative roentgenographs at the time of the accident showed advanced roentgenological signs after ten weeks.

With the more extensive lesions in the Bantu permanent disability up to 20 per cent in certain cases may be expected. It should however, be remembered that spontaneous resolution in mild cases may occur.

The temptation to dismiss a case of knee injury as trivial if no roentgenological signs are found must be avoided, particularly in view of the rarity of lesions of the semilunar cartilages in the Bantu.

The importance of this aspect of knee injuries can not be too strongly emphasized.

ROBERT P. MONTGOMERY, M.D.

Simon, H. E. and Sacchet, H. A.: Muscle Hernias of the Leg. Review of the Literature and Report of 12 Cases. *Am. J. Surg.*, 1945 67: 87.

The observation in 12 cases of muscle hernias of the leg form the basis of this report. Twelve case reports are given with a discussion of the etiology, symptoms and findings, the diagnosis, the differential diagnosis, the treatment, and the prognosis.

Muscle hernias of the leg are not of infrequent occurrence particularly in active young males as represented by soldiers. Such hernias are characterized by a soft, semifluctuant swelling which increases in size when the limb is dependent or the muscle is relaxed, and decreases in size or disappears when the leg is passively elevated and usually when the muscle involved is contracted. It is reducible on pressure, when a distinct fascial defect can be palpated.

There are three types: those due presumably to congenital defects, those due to direct trauma or to indirect muscle violence (usually single, large, and producing symptoms for which surgery is indicated) and the idiopathic type which appears spontaneously particularly after muscular activity is increased. The last type is usually small, often multiple, presents less severe or no symptoms, and frequently requires no treatment.

Conditions to be differentiated from these muscle hernias are localized varicose veins, lipomas, angiomas, and other tumors. Surgical treatment consists of reduction of the herniated muscle and repair of the defect, usually by fascia transplant or suture.

EMIL C. ROBITZKE, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Mowlem, R.: Cancellous Chip Bone Grafts; Report on 75 Cases. *Lancet*, Lond., 1944, 247-745

Seventy-five cases of cancellous chip grafting for the restoration of contour and of continuity in fractures of the facial and cranial bones, the mandible, and the tibia are reported. The results in all were successful, in spite of potential infection in some of them.

In all cases the graft is derived from the ilium. This bone is chosen for its relatively high cellular content and for its porosity. The fragmentation is designed to increase the surface area of the transplant and thus to create optimal conditions for survival of the greatest number of bone cells. The advantage of increased simplicity of the operative technique, although important, is secondary.

The ilium is exposed by an incision about 3 inches long, and its crest and outer plate are freed from their muscular and aponeurotic attachments. Occasionally this process is continued on to the inner aspect. A block of bone of sufficient bulk is then removed with an osteotome, and its cortical covering is discarded. The remaining cancellous mass is divided into chips of various sizes, usually about 1 by 0.5 by 0.3 cm. Irregular shapes are often useful, but it is undesirable to make the chips too small because excessive condensation is likely to occur.

The application of this principle may necessitate alternative methods of bone immobilization, but it simplifies operation and ensures much more rapid regeneration than the accepted methods of bone grafting.

The immediate survival of a bone graft probably depends on the establishment of a blood supply to its

contained cells sufficiently early to ensure their continued activity.

For mechanical reasons, this is unlikely to occur in cortical bones but is much more likely to do so in cancellous bone.

Fragmentation of the cancellous bone renders a greater proportion of its cells accessible to the blood supply and expedites its survival.

A considerable experience in the use of massive cancellous grafts from the ilium pointed to the probability that this type of bone survives from the beginning. The two most important facts underlying this belief are (1) the rapidity with which structural adaptation occurs, so that a new cortex is well marked on roentgenographic investigation in from eight to twelve weeks, and (2) the very high tolerance to infection which these grafts possess as compared with that of the more usual compact graft from the tibia.

GRAFTS FOR THE RESTORATION OF CONTOUR

The basic technique is always much the same. The graft depends for its survival on the blood supply and not on contact with existing bone. The correct contour is obtained by simply building up chips to the requisite levels. Fixation with a pressure bandage for from four to six days completes the procedure.

In all these cases operative technique has been much simplified, in that wide exposures, bevelling of cranial margins, accurate templates, tedious shaping of one-piece grafts, and difficult fixations have been eliminated. In their place is a restricted wound of access, and contour is regained by merely adding or subtracting the requisite number of bone chips.

GRAFTS FOR THE RESTORATION OF CONTINUITY

Thirty-six mandibular defects have been treated in which the loss has varied from $\frac{3}{4}$ inch to half the jaw the average being 3 inches. The bone ends are immobilized by dental cap splints or external bone pins, or both. Eburnated bone and scarred soft tissue are widely removed. The first step in the insertion of the graft consists in placing a distance piece of cancellous bone, about $\frac{1}{4}$ inch thick and $\frac{1}{4}$ inch wide, into position on the deep aspect of the bone ends. This has a twofold function—it prevents soft tissues from bulging out through the mandibular defect, and it protects the chips from movement transmitted from the floor of the mouth. The chips are then laid into position overlying the distance piece and overlapping the mandibular ends, and are arranged to produce the necessary contour. No fixation other than suture of a layer of subcutaneous tissue is carried out, and it is sometimes desirable in the presence of free oozing to insert a drainage-tube for forty-eight hours. Three of these grafts were carried out in the presence of a known opening into the mouth, and many within a few days of the cessation of discharge. None were lost. The average time between operation and the removal of all splintage is 26.75 days, and it must be stressed that the chips

themselves confer no mutual stability whatever. X-ray control shows that fusion begins to be visible between the chips and with the mandibular ends in about fourteen days and continues until the bone is almost indistinguishable from the normal mandible. Clinical rigidity precedes complete roentgenographic fusion, so that careful examination and not x rays are used to determine the point at which fixation can be discarded.

Five cases of extensive losses in the long bones, each associated with an overlying skin defect, have been treated on the same lines. Replacement of the skin defect has usually been the first step although this may sometimes be combined with the bone-grafting operation. In the limbs treated to date, sufficient control of the bone ends was conferred by previously applied plaster casts, and a window was left, through which access was obtained and this was closed at the end of the operation by a further application of plaster. This may not always be sufficient and actual skeletal fixation will then be needed. If this is so either some form of skeletal splintage or a modified bony internal fixation may be used to confer stability. The chips can then be added to produce new bone.

It must be pointed out that the distance pieces are cancellous strips less than $\frac{1}{4}$ inch thick, and that they in no way correspond with the usual type of alar graft. They are simply forms between and around which the contour of the bone is built up with chips. They do not even fit snugly into their slots in the bone ends and they are neither wired nor tied in position. It will be seen that the bone ends themselves are not only cut back to eliminate burned tissue, but also bevelled to provide the maximal bleeding surface for adhesion to and vascularization of the grafts. It is unnecessary and undesirable to jeopardize the blood supply to the bone ends by stripping back of the periosteum through which nutrient vessels pass and it is not justifiable to use power-driven saws or burns because they may create sufficient heat to damage the vessels and the bone cells, on the immediate response of which the whole process depends.

In the tibial cases the initial plaster was removed at the end of five weeks and replaced by a below the-knee walking plaster. This is done in an endeavor to ensure an early return to vascular normality in the limb. The time of removal of all splintage seems to vary with the length of the defect with the degree of vascularity obtained in the bed and with the stresses to which the graft will finally be subjected. A tibia with a 1 inch defect became rigid in ten weeks, while 2 other tibias with defects of more than 4 inches in length are still slightly springy at twelve weeks. In a personal communication Plewes, who has applied this principle to a number of cases of nonunion of the tibia radius, and ulna, without gross loss of bone, reports that all splintage has been discarded in a little less than seven weeks.

X-ray control in the tibial series here reported shows that the chips fuse with equal rapidity at the

ends and in the middle of the defect, but that those chips lying immediately beneath the surface, where the blood supply is indifferent, do not fuse as fast as those in the depths of the wound which are in contact with vascular muscle bellies.

It will be appreciated, therefore that in using cancellous chips the accepted standards of bone grafting are reversed. Instead of splinting the defect with a dense almost noncellular transplant which may also act as a bridge for osteogenesis or as a poor source of new bone—and for neither of these purposes is it histologically suitable—other methods of fixation are used and the defect is filled with a cellular mass, the survival of which will produce the requisite amount of new bone within a matter of weeks. The cases here reported appear to show that such a change of outlook is rewarded by increased operative simplicity decreased postoperative recovery time, and added certainty of results.

ROBERT P. MONTGOMERY M D

King, D : Internal Fixation for Lumbosacral Fusion. *Am J Surg* 1944 66 357

Recently the number of patients operated upon for the removal of displaced intervertebral-disc substance has increased tremendously and it has become apparent that some of these patients should

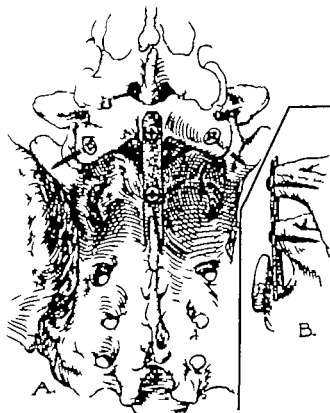


Fig. A, Posterior view of lumbosacral joint showing screws through lateral articulations and tibial graft secured to spinous processes. Multiple chip grafts are not shown. B, Lateral view showing tibial graft.

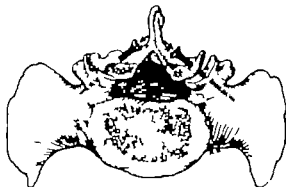


Fig. 2. Sacrum and arch of fifth lumbar vertebra (from above) illustrating direction of sacra.

be subjected to spinal fusion at the same time. Unfortunately the prolonged bed rest in plaster has always been a serious objection to the operation and deterred many people from it. The purpose of this article is to describe an operative technique for fusing the lumbar and lumbosacral regions which furnishes immediate rigid internal fixation and thus eliminates the necessity for external fixation and prolonged bed rest.

The patient is placed prone on a hinged table and the lumbar lordosis is partly obliterated by lowering of both the head and foot ends of the table. The midline incision extends well down over the sacrum so that the muscles can be detached from the dorsal surface as far laterally as the posterior sacral foraminae. With a sharp elevator the muscles and ligaments are quickly and completely cleared from the fifth lumbar spinous process and laminae, and partially elevated from the fourth. The latter maneuver is necessary to get good exposure of the fifth process. Interspinal and supraspinal ligaments, and all other soft tissues are carefully removed from the area to be fused. The lateral articulations are exposed by dissecting and scraping away of their posterior capsular covers and slight opening of their joint spaces by strong traction with bone hooks under the laminae. As much as possible of the



Fig. 3. Case 1. Roentgenograms taken fourteen months after operation. Right, Shows excellent posterior bony bridge.

articular cartilages is removed and then a flat, thin, flexible cautery tip is inserted into the joint and the remaining cartilage cauterized. The fifth lumbar spinous process is removed and put aside for use as graft material at the close of the operation. The sharp edge of the small osteotome or a small gouge can be used to make a notch in the middle of the cortical surface of the inferior articular facet of the fifth lumbar vertebra for the reception of the tip of a No. 31 drill. This is necessary to prevent "wandering" of the drill point when it begins to rotate. If the drill is directed downward and outward parallel to the inferior edge of the fifth lamina (Fig. 1), the resulting tunnel will pass through the middle of the two facets that make up the joint and on into the lateral mass of the sacrum (Fig. 2). A "vitallium screw" is placed in the tunnel and tightened, and the same procedure is carried out on the other side. Rigid lumbosacral fixation can be demonstrated by seizing the stump of the fifth lumbar spinous process with a heavy Kocher hemostat and lifting up and

The remainder of the operation consists in elevating multiple small bone chips from the fifth laminae

*For women and small men X (back long); for large men — back long

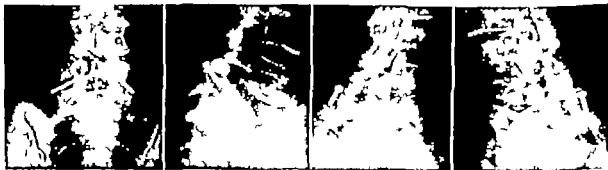


Fig. 4. Case 2. Roentgenograms taken one year after operation. a, Anteroposterior arrow marks site of laminectomy. First two films are left and right oblique

views (60 degrees) to show the lateral articulations. Note complete disappearance of joint spaces. (Courtesy of American Journal of Surgery.)

and the dorsal surface of the sacrum. Supplemental bone grafts from the ilium or tibia are always used by the author ilial bone being preferred. In an occasional case in which the spinous processes are well developed, a tibial graft has been fastened directly on top of the stumps (Fig. 1) with short vitallium screws. After closure several drain pads are snugly strapped over the wound with adhesive, but no brace or cast is used.

The patients are allowed to move about at will. Since internal fixation is rigid the amount of pain is minimal. Many of the patients are up and about in ten days, but the average is about three weeks.

In 1 patient there was persistent burning pain in the distribution of the fifth lumbar nerve root on one side which necessitated the removal of the screw. In a series of 30 fusions the authors have had one postoperative infection. The screws and grafts were removed during the second postoperative week. Three case reports are presented.

ROBERT P. MONTGOMERY M.D.

White, J. W., and Strubbs, S. G. Jr.: Growth Arrest for Equalizing Leg Lengths. *J. Am. M. Ass.*, 1944, 126: 1146.

The procedure presented in this report has been in use for ten years by the authors and has been found to be a simple and effective means of arresting the longitudinal growth of bones. In a series of 140 cases arrested before 1943 there were 302 separate growth arrests, the arresting of both bones below the knee being called one arrest procedure. Since that time more double arrests have been done, almost half the cases having had growth arrests both above and below the knee.

The operation employed in this series consists of the removal of a square core of bone and epiphyseal cartilage from the lateral and medial aspects of the distal or proximal end of the bone attacked with a slightly modified one half inch-square mortising chisel. The chisel is driven into the cancellous bone diagonally over the epiphyseal plate, a skin needle being used as a direction finder. The epiphyseal plate, if the operation is done correctly should divide the excised square plug of bone diagonally in halves. After being driven sufficiently deep the instrument is manipulated so that the square plug of bone breaks off in the depth of the hole, and the chisel containing the plug is extracted. The parts of the plate adjacent to the hole are thoroughly curetted, and the chisel still containing the plug is rotated 90 degrees from its original position and inserted into the hole. With an obturator the plug of bone is driven out of the chisel into the hole. Thus the fragment of the epiphyseal plate in the plug of bone is rotated 90 degrees from its original position which produces a deep bone graft bridging the cartilaginous gap. This procedure is carried out on either side of the femur or tibia but the fibula needs to be attacked only from its lateral aspect. The joint is immobilized in plaster for a period of three weeks.

In order to record discrepancies in leg length more accurately than can be done with a tape measure, x ray films of the patient's pelvis are made with his feet forced firmly down against the foot board at the end of the Bucky table and a standard tube distance. The difference in height of the femoral heads from the transverse foot board is recorded as the difference in length of the legs. The same error is present in all the films and as all calculations are based on these films the error cancels itself. These films have proved to be valuable and accurate records.

A simple method of calculation sufficiently accurate, in the face of so many variable factors associated with bone growth is presented. Regardless of the age and sex of the child the authors calculate that a growth arrest procedure at the distal femoral epiphysis will retard growth at the rate of $\frac{3}{8}$ inch a year while at the proximal end of the tibia and fibula it will retard growth $\frac{1}{4}$ inch. They figure that growth ceases in boys at seventeen and in girls one year earlier. These figures have proved sufficiently accurate in a large number of cases. These methods of calculation and of keeping records, as well as the operative procedure are recommended because of their effectiveness and simplicity.

JOHN L. LUNDQUIST M.D.

FRACTURES AND DISLOCATIONS

Sirls, I. E.: External Pin Transfixion of Fractures; An Analysis of 59 Cases. *Ann. Surg.*, 1944, 120: 911.

The author reports the results of his experiences with the use of external pin fixation in the treatment of 80 cases of fractures during the past three and one half years at the Bellevue Hospital in New York. He believes that the high incidence of discharge around the pin sites alone is sufficient reason to preclude the use of the method as a routine procedure. Many of the infections around the pin sites might have been averted by laying less stress on ambulation and mobilization of the joints, by immediate immobilization of the extremity and pins in plaster and by the application of a new encasement when the swelling had subsided. The high mortality in hip fractures might have been prevented by the use of internal instead of external pin fixation. In the author's opinion external pin fixation should not be used in the treatment of fractures of the hip. External mechanical fixation with plaster is useful if it is restricted to certain problem fractures in which conservative treatment will not give a satisfactory clinical result.

The author calls attention to the fundamental principles in the application of external pin fixation which have evolved as a result of the use of this method by proponents, and as a result of his own experience. He describes the procedure of reduction for simple and compound fractures, the complications, the incidence of infection at pin sites and the time required for these sites to heal the relation

of the healing time of the fracture to the time required for the pin sites to heal, the time required for the healing of fractures treated by external pin fixation, and the indications for the use of external pin fixation.

A number of illustrations and several tables accompany the article.

As a result of his experience with these 80 cases the author believes that the high incidence of discharge from the pin sites (46 per cent) of osteomyelitis of the pin sites with persistence of discharge long after the fracture had united (22.5 per cent) and of death (10 per cent) should preclude the further use of the method as a routine procedure for fractures of the long bones and of the neck of the femur. The procedure should be used only in selected cases, and by those who have been especially trained in the technique. The potential danger of infection at the sites of the pin insertions transcends the dangers of distraction, delayed union, and nonunion. The method should be restricted to certain problem fractures and to persistently displaced compound fractures in which, by visual manipulation, the reduction can be facilitated and maintained until a properly fitting encasement can be expected to maintain the realignment of the fragments. Ambulation and early mobilization of the joints should not be the motivating factors for the use of external mechanical pin fixation.

Infection of the pin sites with distraction and delayed union are attributed to (1) ambulation and motion of the joints without plaster (2) function of the soft tissues against a pin which causes the infection and osteomyelitis (3) pressure necrosis of the bone caused by a pin which impairs the stability of the fixation this permits a continuous hyperemia of the fracture site with absorption of the ends of the bone, and results in distraction of the fragments (4) the prolonged use of the pins (5) failure to immobilize adequately the extremity and pins in plaster and (6) failure to reapply a more snugly fitting encasement when the swelling subsides.

ERIC C. ROSSITER, M.D.

ORTHOPEDICS IN GENERAL

Parkins, J. E.: The Epidemiology of Poliomyelitis. *N. York State J. M.* 945 45 159.

The present knowledge of the spread of poliomyelitis is similar to what we knew about eighty years ago with regard to cholera and typhoid fever. At that time physicians concluded that cholera and typhoid fever were caused by drinking water polluted by the excreta of infected individuals. This theory proved to be a fact years later when the cholera and typhoid-fever organisms were discovered.

Poliomyelitis is caused by a filtrable virus. In the absence of a suitable laboratory animal considerable difficulties have been encountered in direct laboratory experimentation. Most of our knowledge of the spread of poliomyelitis depends entirely upon epi-

demologic evidence. There are apparently several ways of spreading poliomyelitis. The usual manner of spreading poliomyelitis is discussed in this article. In order to understand the epidemiology of poliomyelitis it has to be borne in mind that only a small number of cases affected by poliomyelitis develop paralysis. In areas where poliomyelitis appeared in epidemic form the virus was found in the stools of many persons who had never shown any symptoms of paralysis. Another interesting observation in connection with susceptibility to poliomyelitis is the observation that in a community that had once been affected by this disease new cases of poliomyelitis are very rare. The same condition could be observed in the case of measles and other diseases with a high rate of infection and with a high degree of immunity resulting from the infection.

It has been accepted that the disease is spread by man himself. It is conceivable that the virus might be harbored by animals and insects under certain unusual circumstances. The actual portal of entry in poliomyelitis is the pharyngeal mucosa, and at times the lower intestinal tract. Faber, Silverberg, and Dong reported that in their experiments with cynomolgus monkeys, invasion of the central nervous system had been via the trigeminal nerves and via the sympathetic fibers of the nasopharynx. The peak of poliomyelitis usually occurs in the summer when also certain insects are prevalent. It must be stressed, however, that the prevalence of the infection in summer time does not exclude person-to-person spread of the disease. Although poliomyelitis is rarely seen in the cold season, the statement that poliomyelitis disappears as soon as there is a frost is not correct. Another factor in doubting that poliomyelitis is usually spread by insects is the fact that malaria, a disease known to be spread by insects, does not follow the clinical, laboratory, and epidemiological pattern of poliomyelitis. The poliomyelitis virus has been demonstrated on flies. These flies apparently come in contact with human excreta. The fact that the elimination of horse stables and privies in larger cities did not eliminate the disease indicates that flies have very little bearing on the spread of the disease. It has been clearly shown that water has no influence in the outbreaks of poliomyelitis in certain regions. In the years 1916 and 1915 it was found that raw milk was the means of transmission of poliomyelitis in only 7 or 8 cases. Since that time a considerable amount of evidence has been accumulated to show that milk is not usually involved in the transmission of poliomyelitis.

In considering the transmission of the disease through person-to-person contact, it was frequently possible to demonstrate the radial spread of poliomyelitis. This has been observed in many other respiratory-spread diseases, for example, measles. The fact that poliomyelitis is more frequently seen in rural communities might be explained by the fact that in larger communities the encounter with a poliomyelitis virus takes place at an early age. It is likely that for this reason there is a certain amount

immunity against the disease. In smaller communities there is less contact between individuals, and the first encounter with this disease usually occurs at an older age.

In considering effective control measures, based upon the theory of person-to-person spread, rigid isolation of the affected individuals would be indicated. The effectiveness of this program is limited when one considers that ordinarily only analytic cases are reported to the Health Department. These cases, however, account for only a small portion of affected persons, and by the time because is reported the patient usually has had ample opportunity to spread the disease. Parents living in the affected areas are advised to keep their children from gatherings and to avoid contact with children that show any signs of illness. Overfatigue, chilling, and tonsillectomy should be avoided in an area in which poliomyelitis is occurring. From a scientific point of view there might be some doubt as to the wisdom of postponing the first encounter with the virus for adulthood. Effective control of poliomyelitis would be accomplished through a safe vaccine. Unfortunately the methods employed to kill the virus in the vaccine also destroy its anti-toxicity.

Investigators in Chicago have developed an effective vaccine against the homologous mouse adapted Lansing strain. This vaccine was produced by a newly developed method of ultraviolet light irradiation. Before accepting this vaccine over enthusiastically for human beings it must be tried on many more mice and many more monkeys and on many more strains of poliomyelitis. It is possible that in a few more years the problem of poliomyelitis may be solved by active immunization.

GEORGE L. REESE, M.D.

Logan, L. S.: Practical Points in Plaster Techniques; Two Years of Experience in Forward Surgery with a Royal Army Medical Corps (Mobile) Casualty-Clearing Station 1941-1943. *Surgical New Zealand J Surg.*, 1944, 14, 75.

The surgeon in forward areas fulfils two main functions: (a) the saving of life from immediate and grave battle injuries, and (b) the treatment of many other wounds, chiefly injuries to muscles and compound fractures. The first function will occupy some 75 per cent of his time. The permanent relief of pain and the minimization of sepsis in an already infected wound stand out prominently among the objectives of surgery as practiced in a casualty-clearing station. The surgeon there needs few instruments and little academic knowledge, but above all he requires experience. With experience come many tricks of the trade which make his work easier and more effective. Complete immobilization may be regarded as the keynote of all. It banishes pain, overcomes shock, lessens sepsis, and allows healing to begin while the patient is still far from a base hospital where more effective measures are possible. Complete immobilization is just as necessary for

fractures or injuries of the muscles and skin as it is for those of bone.

Loose army plaster of Paris This is the most useful of all. It is easy to carry in bulk, is of good quality and is easy to make up into bandages of any width. It is slightly slower in setting than Cellon, and is cheaper. Indeed the best plasters were made from alternate bandages made with loose plaster of Paris and Cellon.

A plaster must be strong to serve its purpose. Often on the arrival of a convoy broken and, therefore pain producing plasters were observed. Lower limb plaster cases usually break just about the ankle or just below the knee and they should therefore, be made stronger in these locations. Greater strength in these locations is required in a plaster used for travelling than in one put on at a base hospital.

Slabs are always broken and are therefore mentioned only to be dismissed.

Adequate length is another important feature. Many plasters are too short, and as a result do not fulfil their function. Many patients come with the toes unsupported and therefore are subject to pressure from the blankets. Plasters for the lower leg arrive with the plaster prolonged about 4 inches above the knee. This part usually softens and, the limb having shrunk a little, movement at the knee readily takes place. It is better therefore to carry these plasters higher—indeed as a routine up to the groin—in order to avoid a painful limb. Application from the groin to beyond the toes is advised.

Adequate padding is also important. Opinions on this subject differ markedly and the author's casualty-clearing station has undergone a reversal in technique from the completely skin-tight closed plaster to a split, lightly padded cast. The artistry of the nonpadded cast has given way to the safety of the padded cast. They have however always used felt over the heel and the malleolus; particularly the heel, for it is of little avail to have the tibia and fibula united at the end of ten weeks if the slough over the heel has not yet separated. It is thought better thus to play for safety for once the patient leaves the casualty-clearing station the delays may be of almost any length until the next hospital or medical area is reached. When wool is not available, split Gamgee has been used. It is not so good but can be made to answer the purpose.

Finally a plaster must be easily and painlessly removable. Such incidents as the swelling of a limb at a bony point becoming painful or some similar misfortune may arise at any time and call for immediate removal of the plaster cast. Padding prevents unshaven hairs from sticking to the plaster and the use of the greased pig makes splitting and therefore removal easy. The greased pig is a thick round rubber tourniquet liberally smeared with vaseline which is laid on the limb after the limb has been covered with wool. The plaster is now applied in the usual way over the tube and when it has just set the tube is pulled out, an elevated tunnel thus being left down the whole length of the cast. This is cut open

at once, 2 inches being left intact at each end for the purpose of holding the ends of the plaster together. Should now an urgent removal of the plaster become necessary it is a simple matter to cut the two ends. The splitting of the plaster allows of expansion of the limb to minor degrees, and thus makes the cast safer without the loss of any of its powers of immobilization.

Each patient in plaster should be kept at the station for two days if possible. The first day is for thorough drying and setting, and the second to make sure that the plaster is comfortable. Every complaint about pain in a limb in plaster should be listened to. Pain means that something is wrong, and when pain is present plasters should be reapplied until they are comfortable.

The chief causes of trouble in plasters for wounds of the hand and wrist are the slabs are too thin and break at the wrist they are not molded around the arm to grip it they do not in certain cases extend beyond the finger tips to protect them against jarring, and circular plasters cause stiff fingers and often swelling beyond. To avoid these troubles, the wound is attended to in the usual manner and a wet, shrunk bandage is applied around the arm down to the hand. A thick, long, wide slab is made and applied over the volar surface of the arm from just distal to the elbow joint to well beyond the finger tips. It is molded around the arm and into the palm, with the hand slightly dorsiflexed. The piece projecting beyond the finger tips is then bent back dorsally and heaped up to form a small bar just distal to the finger tips. The rest is molded back to strengthen the wrist part. The rim thus formed distal to the finger tips prevents movement, and injury and makes a comfortable support in which the fingers can move if this is desired. A cast of this type is extremely useful in all inflammatory infections of the hand, and is recommended for these it can be modified to suit conditions. However in the main it stops pain, limits infection, and allows early resolution.

PLASTERS FOR FRACTURES IN THE LOWER LIMB

To avoid the usual troubles a plaster cast is applied in the following manner:

The limb is held in abduction, extension, and slight flexion at the knee, with the foot in planter flexion. Cotton wool in rolls is applied from the groin to the toes. Three pieces of felt are held ready one for the heel and one for each malleolus. The greased tourniquet is laid lengthwise down the limb over the wool, the metal end being caught between the first two toes and the other end being left at the groin. The plaster is applied first at the thigh and a strong and adequate case is made. A pause is made after the knee is covered so that the plaster may set with the knee in slight flexion. The rest of the plaster is then applied to the toes, the heel traction being kept up and care being taken that the foot is in the neutral position. A slab is now made about 20 inches long, out of two 6-inch bandages. It is applied to the back

of the calf and up to the toes, so that 6 inches overlap the toes on the dorsal aspect. The slab is bound to the cast up to the toe level, after which the 6-inch overlap is turned back to the planter surface, the slab thus being doubled and a shelf being left projecting 1 inch beyond the toes. A small slab of "Cellon" about 10 inches long, made from 4-inch bandage, is laid across the end of the major slab. The ends of it are then brought down on each side of the foot. The plaster is finished with one 4-inch bandage. This plaster is an adequate one, the toe cap never breaking. The toes should be seen to be capable of full movement.

PLASTERS FOR LARGE WOUNDS OF THE THIGH AND FRACTURED FEMUR

From a casualty-clearing-station standpoint, the only type of immobilization which has stood the test of desert travel is the "Tobruk plaster." Immobilization is the only principle of importance as far as the casualty-clearing-station treatment of fractured femur is concerned. The Tobruk cast produces the best immobilization possible, and therefore extension is unnecessary in the author's opinion. Some still desire it and therefore it has been included in the technique.

The wound is attended to and dressed. A suitable Thomas splint is chosen and bent at the knee, and slings are made. For those who desire extension, the leg is shaved and strapping is applied from the mid-thigh to beyond the toes, padding being put between the strapping and the malleoli. The whole limb is padded with wool and a complete plaster is applied from just distal to the groin to the toes, the knee being included in a slightly flexed position, the toes with a good stout toe support, and the foot in a neutral position. A "greased pig" is used to allow of splitting. A felt pad is placed under the heel. The encased limb is now put into the Thomas splint. The ring is pushed well against the ischium and well into the adductor region. Care is taken that the bend in the Thomas splint corresponds to the flexion of the knee. Three shell dressings are now used. One is pushed between Scarpa's triangle and the ring, and the other two are placed between the outer aspect of the thigh and the ring. The ends of the extension strapping are now tied and fixed to the end of the Thomas splint by a cord. A Spanish windlass is inserted and twisted tight. The leg encased in a complete cast is now fixed immutably to the Thomas splint by three 4 inch "Cellon" bandages. One is placed at the ankle, one at the knee, and one at the ring, the shell dressings being first taken in so as to fix them. The "greased pig" is withdrawn and the cast is cut, the customary 5 inches being left at each end. A Sinclair's footpiece (the iron hoop) is now firmly fixed to the end of the Thomas splint by a plaster bandage. This does away with the stretcher bar and allows the patient to be nursed in bed and handled easily in air transport. It supports the splint and the limb perfectly when its foot is put between two folded blankets.

In the case of fractures of the femur, high in the shaft or at the neck, the author has used a technique similar to that described, but has prolonged the cast proximally so that it follows the line of the groin to the iliac crest, thus grasping the trochanter. The ring of the Thomas splint in this case will not slip over the proximal end of the plaster but rests on it. Any attempt, therefore, at extension is impossible. This method combined with the use of a stretcher bar, to anchor the distal end of the limb firmly allows the patient to travel comfortably.

The points in favor of this method are

1. There is no rotation of the limb inside the plaster for the limb and foot are encased
2. The foot cannot drop or twist and the toes cannot become painful because all are supported at the same time free toe movement is allowed
3. The raw surfaces of the wound itself are given immediate support.
4. Practically no hip-joint movement can take place if the end of the spint is fixed.
5. The method is simple, quick, and always has been efficient in the author's experience.

PLASTER FOR WOUNDS OF SHOULDER GIRDLE AND HUMERUS THE THORACOBRACHIAL CAST

On the patient's arrival, an anesthetic is given the wound is treated and dressed and the limb is bandaged to the side of the chest wall with a strong band bandage, the arm being kept in flexion. Next morning the following preparations are made.

One hour before the patient is brought to the theater morphine ($\frac{1}{4}$ gr) and scopolamine are given. A further dose of morphine is given intravenously. The patient's co-operation is sought by explanation as to the procedure. He is made to sit up in the stretcher and the bandage over the forearm put on the night before is cut off. The forearm is now bandaged with the wet bandage and a good volar slab is applied to the heads of the metacarpal bones. This is allowed to set hard being the permanent hand support. The patient is now made to sit on a stool. His feet are widely spaced to get a good base, with someone holding his hand firmly. The rest of the previous night's bandage is removed quickly the whole arm being freed and incidentally considerable pain is caused for the time being.

A large pad of felt is applied over the injured shoulder girdle, care being taken that it covers the

spine of the scapula, the lateral aspect of the humerus, and the clavicle. Three shell dressings do equally well for this purpose. Over the olecranon a thick felt pad is applied and everything is bound on, two rolls of cotton wool being put in the gutter between the chest and the arm. The author uses two 6-inch bandages for this in a modified Velpeau technique. The arm is kept flexed with the elbow brought forward toward the midline. The forearm is kept free from the bandage and is kept held with a slight forward rotation to allow room to work between it and the chest wall.

The plaster is now applied a triangle being made with the base extending from the base of the neck to the olecranon on the injured side, and with its apex under the opposite axilla. Slabs are used to strengthen this. One extends from the base of the neck to the olecranon and embraces it. The other extends from the vertebral groove, passes around and forward to wrap around the lower and outer third of the humerus.

The whole humerus is now completely encased and all that remains is to fix the forearm by means of a plaster sling in a flexed position over the front of the chest. With a 6-inch bandage a start is made over the injured shoulder a sweep is made downward over the flexed forearm, underneath it, and then up under the opposite axilla, and so on to the original starting point. Three bandages suffice for this purpose.

At this stage the patient is no longer in pain. In contrast to his former condition one of considerable anxiety and pain he can now get up and walk away if too much morphine has not been given to allow it.

The fixation of the humerus. Additional points of importance in the fixation of the humerus are the following

The apex of the plaster under the opposite axilla should be made narrow and firm. The cast should be kept as high as possible, so that it does not chafe the abdominal wall when the patient is in the sitting position. There should be free movements of the fingers and support for the hands. The whole cast should fit snugly and allow little or no movement between the body and the cast.

The application of a thoracobrahial cast is the most dramatic procedure a casualty-clearing station ever does for a conscious patient.

ROBERT P. MONTGOMERY M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Fleming, B. J.: Mesenteric Vascular Occlusion. A Presentation of 15 Cases. *Am. J. Surg.* 1944, 66: 68.

Since 1895, when Eliot reported the first successful resection of the small intestine for mesenteric thrombosis, each year adds several reports of cases on this subject. This disease has a comparatively low incidence. A study of the literature on mesenteric occlusion reveals that the number of cases cannot be tabulated exactly.

To date it appears that about 554 cases of this disease have been reported in 32 of which resection was successful. At Kings County Hospital, Brooklyn the author encountered 5 cases during his surgical service. Further investigation revealed that 10 cases diagnosed at autopsy or at operation, had been recorded at Kings County Hospital from January 1935 to December 1943 which gave 15 new cases. Among these cases 3 operative survivals are recorded. This brings the total number of successful resections to 35.

As a general statement, it may be stated that the predominating cause of mesenteric occlusion in younger patients is found to be heart disease or infection. In older patients degenerative or premalignant conditions appear to be important etiological agents.

Attempts have been made to outline a clinical syndrome which might serve as a basis for the early diagnosis of mesenteric occlusion. Some believe that venous mesenteric occlusion can be segregated clinically from the arterial type. As it is very difficult to diagnose mesenteric vascular occlusion preoperatively or before death, it can be appreciated how much more difficult it is to differentiate the venous from the arterial type.

The belief that cardiac disease, especially auricular fibrillation, is a prerequisite for superior mesenteric arterial occlusion is not held by the author on the basis of his experience.

No pathognomonic findings are known. The onset of an acute surgical condition of the abdomen in an elderly patient may suggest this disease. Shock is more pronounced than in most other abdominal conditions with the exception of pancreatitis. Pain is out of proportion to the physical findings. Physical findings are usually variable degrees of tenderness, rigidity distention and absence of peristalsis. A previous fallacy was the fact that cardiac irregularities and bloody stools were considered necessary in the clinical picture of this entity.

In this series, occlusion occurred more frequently in the superior mesenteric vessels than in the inferior mesenteric vessels. Conservative therapy in cases of mesenteric occlusion is ineffectual treatment. Surgical intervention with radical resection of the involved

loops (beyond the areas of edema) is the only hope for cure.

The author's mortality rate was as high as that reported elsewhere. This mortality ranges from 60 to 90 per cent, and is due to shock and loss of blood. The author believes that the appalling mortality associated with this disease can be lowered only by improvement in diagnosis.

Treatment is of no avail in those cases in which occlusion of the superior mesenteric artery produces gangrene of the entire small intestine. Treatment is also ineffectual in cases in which the patient's general condition is so desperate (due to shock, heart disease, toxemia, or liver damage) that any operative procedure cannot be contemplated.

JOHN E. KIRKPATRICK, M.D.

Imler, A. E., Beaver M. G., and Sheehan, W. G.: The Value of Venography in Varicose Veins. *Am. J. Roentg.* 1944, 52: 5-4.

Venography is a valuable aid in the diagnosis and treatment of the following vascular diseases of the lower extremity: thrombophlebitis, pulmonary embolism, arteriovenous fistula, venospasm and varicosities.

The authors in this report are concerned with the efficacy of venography in selected cases of varicose veins. Ten per cent of healthy adults suffer from superficial varicosities. Before obliterating the superficial veins it is taken for granted that the deep veins are patent. The standard examinations (Perthes and bandage tests) for patency of the deep veins will prove adequate in the great majority of cases. However in order to prevent the recurrence of varices, a careful consideration must be given to the existing conditions. Recurrent varices may be due to technical errors or deep venous obstruction and stasis. Superficial varicosities associated with deep venous obstruction are compensatory and their obliteration will be promptly followed by a recurrence. In such instances the clinical patency tests may be normal and as a result may be misleading.

As contrast medium, a 35 per cent solution of diodrast is used. All patients are tested for diodrast sensitivity. Although the technique is not described in this article, it has been thoroughly described in a previous article (Papper, E. M., and Imler, A. E. *Surgery* 1944 15: 403). Three cases are reported in detail.

It is the opinion of the authors that positive evidence in venographic studies will defer surgical interference that might result in a permanent aggravation of symptoms and a recurrence of varicosities. Venograms are indicated in those patients suffering from varicose veins with a history of thrombosis or thrombophlebitis, pain and fatigue on walking or standing, edema or symptoms of orthostatic collapse, or major vascular anomalies.

MAURICE D. SACHS, M.D.

Shapiro, M. J. The Preoperative Diagnosis of Patent Ductus Arteriosus. *J Am M Ass* 1944, 126 934.

The author notes that since it is now possible to cure a patent ductus arteriosus by surgery it is of almost importance that the correct diagnosis be made, lest patients be subjected unnecessarily to a major surgical procedure or those with this lesion be denied the possibility of surgical cure. Two types of patency of the ductus may occur. The duct may remain open as part of a serious developmental defect and be the only means by which the circulation can be carried on in a heart seriously impaired by congenital defects. Such patients have evidence of congenital heart disease. In the type of case which is curable by surgery, the patent ductus is the only defect present, and the heart is otherwise normally developed. Strictly speaking, the uncomplicated isolated patency of the ductus is not a congenital lesion as it occurs after birth and has nothing to do with developmental defects of the heart. In the normal newborn infant, the ductus closes within a few minutes after the first breath is taken. Recent studies suggest that failure of closure in uncomplicated cases of patent ductus arteriosus may result from lack of oxygenation of the blood, possibly because of obstruction of the air passages in the newborn child.

The author discusses in detail the sex and age incidences, the clinical characteristics and the electrocardiographic and x ray findings in the 62 patients in whom a definite diagnosis of uncomplicated patent ductus arteriosus could be made. In 23 instances, there was an opportunity of checking the diagnosis. The diagnosis was correct in each instance.

The diagnostic criteria of patent ductus arteriosus may be summarized as follows: (1) machinery murmur (2) thrill in pulmonary area (3) enlarged pulmonary artery, (4) enlarged and pulsating pulmonary vessels (5) enlarged heart (6) increased pulse pressure (7) stunting of growth (8) absence of cyanosis and clubbing of fingers, (9) normal electrocardiogram and (10) history of heart disease from early childhood.

In the differential diagnosis, several cardiac conditions may be confused with patent ductus arteriosus. One of the most important, especially in infants and young children is the so-called venous hum in which there is also a continuous murmur heard over the base of the heart. It is usually not as loud as the characteristic machinery murmur. Occasionally, the diastolic murmur of aortic regurgitation will simulate the machinery murmur. In aortic regurgitation however there is invariably a pause between the systolic and diastolic murmurs. These murmurs are usually heard lower down along the left border of the sternum.

Patients with interauricular septal defects commonly exhibit x ray changes which simulate the findings in patent ductus arteriosus. On fluoroscopy the contour of the heart may suggest that found in patent ductus arteriosus however in most instances

the heart is considerably larger and more rounded in patients with interauricular septal defects.

In conclusion the author notes that the diagnosis of patent ductus arteriosus can be made without error. Patients should not be referred for surgical treatment unless they show the characteristic machinery murmur. The only exception to the rule is the occasional patient with a large patent ductus who may exhibit no murmur. Patients with cyanosis and clubbing of the fingers do not have uncomplicated patent ductus and they cannot be treated surgically. Pronounced electrocardiographic changes are not a part of the picture of simple patent ductus arteriosus.

HERBERT F THURSTON M.D

Bettman, R. B. and Tannenbaum W. Ligation of Patent Ductus Arteriosus in the Presence of an Apparent Bacterial Endocarditis; Report of a Case Apparently Cured. *Ann. Int. M.*, 1944, 21 1035

The authors report in detail a case in which ligation of a patent ductus arteriosus was done in the presence of an apparent bacterial endocarditis in a young woman eighteen years old. Two years after the operation the girl is well, healthy and to all appearances is living a normal life.

The feasibility of ligation of a patent ductus arteriosus was first demonstrated by Gross. The fact that such ligation in the presence of what appears to be a bacterial endocarditis may result in the cure of the disease was definitely established by Tourouff and confirmed in several other reports. Inasmuch as medicine operates very much as law on the basis of precedent, it will take an accumulation of statistics from many cases before the medical profession in general becomes cognizant of this new therapeutic procedure. Therefore the authors state their purpose of publishing the results of ligation of a patent ductus in the presence of bacterial endocarditis as they observe them.

HERBERT F THURSTON M.D

Nixon, J. W. Surgical Ligation of a Patent Ductus Arteriosus Associated with an Aneurysm of the Pulmonary Artery. *J Thorac Surg.*, 1944, 13 513.

The author failed to find in the literature a report of successful surgical treatment of a case of an aneurysm of the pulmonary artery associated with a patent ductus arteriosus. This fact led him to report the following case.

A nineteen year-old white female was admitted with the chief complaint of dyspnea on exertion and a diagnosis of a patent ductus arteriosus. The patient's past medical history was negative except for a humming and roaring in her chest which was present since early childhood and was more pronounced when she was lying down. She tired easily and when exerting would develop palpitation, dyspnea and precordial pain. Physical examination was negative except for a thrill over the pericardial region and a to-and-fro machinery murmur transmitted to the left axilla and back.

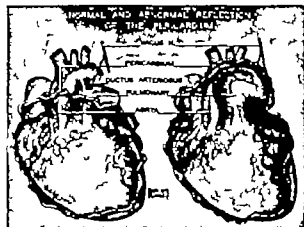


Fig. Left, Position of pericardium as it is normally reflected from the pulmonary artery. Right, Pericardium reflected from the aorta as found in this case.

Laboratory findings were essentially normal. The patient was operated on under intratracheal cyclopropane anesthesia through the usual anterior incision over the left second intercostal space. When the pleural cavity was opened an expansive pulsating mass was encountered within the pericardium extending upward in the region of the aorta. The pericardium, instead of being attached to the pulmonary artery as is usual was attached to the inferior surface of the aorta and thus overlay the ductus (Fig. 1). On incision of the pericardium the mass was shown to be an aneurysm of the pulmonary artery and only after the aneurysm was retracted downward could the ductus be exposed and dissected free. The ductus entered the aorta at a marked obtuse angle—a factor undoubtedly contributing to its patency. When the ductus was ligated with No. 8 braided silk, the thrill and murmur disappeared and the pulsation of the aneurysm markedly diminished which indicated that the blood flow through the ductus under aortic pressure exerted an increased strain on the aneurysm wall. No attempt was made to deal with the aneurysm. The pericardium was closed with cotton sutures and the ribs with wire sutures. The patient had an uneventful rapid recovery with discharge on the eighth postoperative day. There was some laryngeal nerve injury due to the extensive dissection required to locate and free the ductus. The hoarse voice had disappeared by five weeks and the patient was working as a clerk with marked improvement in the dyspnea.

Although patent ductus arteriosus is next to patent foramen ovale as the most common congenital cardiac defect, aneurysm of the pulmonary artery associated with it is rare. Only 11 cases of aneurysm of the pulmonary artery were reported in the literature from 1833 to 1930 and a patent ductus was present in 33 per cent of these cases. The pulmonary hypertension associated with patent ductus has been regarded as a cause of pulmonary aneurysm, but

since patency of this passage is common without aneurysm, it seems reasonable to assume that some additional lesion must contribute to its production. Syphilis has been considered also as an important causative agent.

Dilatation and thinning of the pulmonary artery may be present in cases of patent ductus arteriosus, but a true aneurysm is rare. This amount of thinning seems to depend on the diameter of the ductus and the completeness of its patency.

The failure of a ductus to close at birth is probably due to its position and direction. It usually enters the aorta at a right angle but as the acuteness of the angle decreases it becomes more exposed to intra-aortic pressure. If the angle becomes obtuse, the patency is maintained and a greater pressure and volume of the aortic blood passes into the pulmonary artery the wall of which, not intended for such pressure, may yield to form an aneurysm. The presence of these two associated lesions leads to diagnostic confusion and adds another argument in favor of surgical closure of the recognized patent ductus.

ROBERT BRIGLOW M.D.

Alexander J. and Byron, F. A.: Aortectomy for Thoracic Aneurysm. *J Am Med Ass* 944, 186 1939.

The authors successfully removed an aneurysm of the thoracic aorta measuring 11 by 8 cm. together with a 7.5 cm. length of the aorta. This is believed to be the first case of successful removal of an aneurysm of the thoracic or abdominal aorta or of successful ligation of the thoracic aorta. The patient was a white youth, aged nineteen whose symptoms and physical signs led to a provisional diagnosis of aortic coarctation on the basis of extrinsic pressure by a neoplasm (Fig. 1).

Thoracotomy was performed under intratracheal ether anesthesia and a sacular aneurysm of the upper descending aorta was exposed in the costovertebral gutter. The upper pole was 5 cm. inferior to the left subclavian artery and the attachment to the aorta was about 7.5 cm. long. The pulsations in the aorta above it were strong but those in the aorta below it were only questionably palpable. The aorta at its junction with the upper end of the aneurysm appeared to be slightly constricted. The subclavian internal mammary and upper intercostal arteries were greatly enlarged. As the thin-walled aneurysm was in danger of rupture at any time and as the collateral circulation appeared to be adequate, resection of the aneurysm was decided on. The aorta just below the origin of the left subclavian artery was ligated with a 1.3 cm. wide cotton tape, and a silk ligature was placed between the tape and the place where the aorta was to be divided. The aorta was similarly ligated 4 cm. below the aneurysm. Three pairs of greatly enlarged intercostal arteries emerging from the aneurysmal sac were ligated and the entire aneurysm-bearing segment of the aorta was removed. The divided ends of the aorta were oversewn with silk, and a pedicled flap

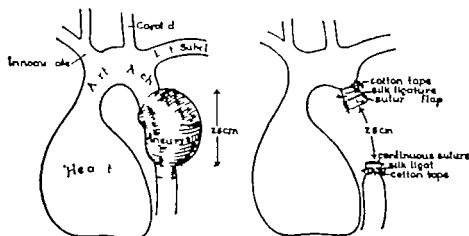


Fig. 1. Before and after resection of the aneurysm. Actually the aneurysm was 11 cm. long. Its attachment to the aorta was 7.5 cm. long.

of the posterior aneurysm wall was turned over the open end of the superior segment of the divided aorta and tacked to the aortic wall (Fig. 1).

The feet remained warm throughout the operation and afterward but there was a postoperative rise in blood pressure in the upper extremities. Acute cardiac decompensation occurred seventeen days after operation and receded rapidly under treatment. Up to three months after operation kidney function tests were consistently normal but there was persistent hypertension with retinal angiospasm, exudates, and hemorrhages. One year after operation the patient's activities were the same as before operation, and examination showed the acute process in the retinae to be at a standstill although the hypertension was still present. Because of the persistent hypertension and angiospasm the prognosis of the condition must be guarded.

This aneurysm probably arose in connection with an aortic coarctation, the presence of which is presumed because of hypertension, a well developed collateral circulation, notching of the ribs and the absence of pulsation of the aneurysm and of the aorta below it. This patient was unique in that all the factors essential to the success of the operation were present: his youth and good general health, the absence of syphilitic disease of the aorta, the presence of a well established collateral circulation, and the location of the aneurysm which permitted the placing of the proximal ligature on the aorta below the left subclavian artery.

JOHN L. LEXQUIST, M.D.

Scott, V.: Abdominal Aneurysms. *Am. J. Syph.* 1944, 28: 682.

In a series of 96 cases of abdominal aneurysm of the aorta or its main branches, 58.3 per cent were syphilitic, 20 per cent arteriosclerotic, and 18.8 per cent mycotic. In 43 of these cases the aneurysm involved a branch of the aorta. Of the latter cases 33 per cent were syphilitic and 18.6 per cent were arteriosclerotic, and in 41.9 per cent the aneurysm

was caused by bacterial agents. Multiple abdominal aneurysms were present in 18.7 per cent of this series and in 30 per cent arteriosclerosis was the causative agent. Aneurysms of the upper abdominal aorta, including those involving the celiac axis and superior mesenteric artery were most frequently syphilitic, while those of the lower abdominal aorta were either arteriosclerotic or bacterial. Arteriosclerotic aneurysms usually occurred in patients over fifty years of age and of the white race; they were predominantly males. Luetic aneurysms occurred mainly in the colored race.

The symptomatology of abdominal aneurysm is dependent upon its size and location. Pain, especially of the nocturnal type, was characteristic in the luetic group. Often it was associated with vertebral erosion. Arteriosclerotic aneurysms were asymptomatic in 80 per cent of the patients. In the mycotic type bacterial infection masked any aneurysmal symptoms. The presence of a pulsating expansile mass with palpable thrill and audible bruit was dependent on the size and location of the aneurysm. In 75 per cent of the luetic group the latter physical signs were detected. In a differential examination it must be remembered that neoplastic or inflammatory tumors close to large arteries may give similar findings. Furthermore intraluminal clotting may cause the thrill and bruit to disappear. The largest sized aneurysms were usually luetic, but in all groups the sacular variety predominated. Rupture of the aneurysm occurred frequently in from 39 to 41 per cent of the mycotic and luetic types—and hemorrhage extended commonly through the retroperitoneal tissues and less frequently into the peritoneal cavity.

Thirty-four per cent of the patients with luetic abdominal aneurysms also gave signs of aneurysmal involvement of the thoracic aorta. Erosion of the vertebra was common in the luetic aneurysms of the upper abdominal aorta. This was usually demonstrated by x-ray examination which also revealed calcium deposits in the vessel walls.

The prognosis of syphilitic abdominal aneurysm was found to be variable but poor. In 70 per cent of the patients death ensued within thirty-six months after the onset of symptoms and only 17 per cent lived more than five years.

As regards treatment, there has been little tendency to treat such lesions. However, Blakemore and Lord have recently offered a promising method of controlled electrothermic coagulation for aneurysms.

BENJAMIN G. P. SHARITOFF, M.D.

BLOOD; TRANSFUSION

Invernizzi, D. and Yannicelli, S.: Distribution of the Rh Factor in the Population of Montevideo (Distribucion del factor Rh en la poblacion de Montevideo) *Arch. surg. med.*, 1944, 5: 85

This article describes the first attempt at determining the frequency of the Rh factor in the blood of the population of Montevideo. The majority of the individuals examined were voluntary donors of blood in the Center for Blood and Plasma. Some determinations were made in the Maternity Hospital with the object of studying a case of fetal erythroblastosis which will be published elsewhere.

The anti-Rh sera used were from two sources. The first was obtained from a woman who gave birth to a child which died of fetal erythroblastosis. This serum contained an irregular agglutinin which was identified as anti Rh. The other was a human anti Rh serum given by the Rockefeller Foundation of New York.

The technique of the reaction is described. Among the 113 determinations, 92 or 81.4 per cent, were Rh-positive and 20 or 17.85 per cent, were Rh negative.

AUMERY G. MORAN, M.D.

Macklin, M. T.: The Diagnosis of Rh Incompatibility Especially by Microscopic Appearances; Its Relation to the Syndrome Formerly Diagnosed as Erythroblastosis. *J. Pediat.*, S. Louis, 1944, 5: 533

Erythroblastosis as originally defined indicates the presence of large numbers of nucleated red blood cells in fetal livers at a stage in development when erythropoiesis should largely be absent from the liver. This is evidenced by the presence in the circulating blood of the fetus or newborn infant, of immature red cells the type or quantity of which is not normal for that stage of development. Rh incompatibility is suggested as the term for the disease entity caused by a reaction between Rh antigens in the fetus and the specific antibodies in the maternal blood to combat them. This results in erythroblastosis due to hemolysis but many conditions other than those involving incompatible Rh factors in mother and fetus are factors in the production of erythroblastosis. The author outlines diagnostic criteria of Rh incompatibility. Many of the criteria said to be diagnostic of Rh incompatibility may be found in other conditions and may not always be found in Rh incompatibility.

In order to diagnose whether a fetus is suffering from Rh incompatibility it must be shown either (1) that the fetus possessed in its circulation antibodies against its own Rh positive cells, or (2) that the blood of the fetus and mother were of different Rh groups and that the fetal tissues showed departures from normal which were characteristic of the antigen-antibody reaction.

Probable Rh incompatibility can be diagnosed in the living infant when different Rh factors are demonstrable in mother and fetus, and an anemia, or jaundice, or both, unexplained by other conditions are present in the infant. The diagnosis is strengthened if other infants in the same family have suffered from fetal jaundice or from proved Rh incompatibility.

Probable Rh incompatibility can be diagnosed in the stillborn infant or in the infant after death when different Rh factors are present in mother and fetus, and when the fetal liver shows that hemolysis has taken place as evidenced by the presence of iron in the liver. This is determined by the Prussian blue technique.

Some of the criteria used for the diagnosis of Rh incompatibility are of value only when the fetus is full term or when the infant lives for several days. They are not of value on fetuses lost early in pregnancy. The iron test is of value in these early cases.

Iron is not normally stored in fetal livers in such form that it is demonstrable by the Prussian blue technique; therefore, iron as revealed by this test indicates excess blood destruction. One of the most frequent causes of such excess destruction is Rh incompatibility.

ERNEST E. ANDERSON, M.D.

Camponovo, L. E.: The Study of Oxalic Acid as a Hemostatic (Contribucion al estudio del acido oxalico como hemostatico) *Rev. As. med. argent.*, 1944, 38: 98.

The author reviews the work previously done on the use of oxalic acid as a hemostatic. Some investigators hold that it does act as a hemostatic, while others deny this property.

He reviews the physical properties of the acid, and its metabolism and pharmacology before he takes up the description of his experiments. A certain amount of this acid is found normally in the blood. The author gave it to dogs by intravenous injection in doses of 5, 10 and 20 mgm. The determinations of the coagulation time were made by the method of Lee and White. A control animal did not show any change in coagulation time in the various tests. Tests made ten minutes after the injection of oxalic acid showed lengthening of the coagulation time in some of the experiments, no change in some, and moderate shortening in others. The details of the results are given. Tests made twenty minutes or later after the injection showed shortening of the coagulation time, with the maximum shortening between fifty and seventy minutes after injection.

Oxalic acid was used clinically in 10 cases of hemorrhage in human subjects due to various causes.

The injections in these cases were made intramuscularly. The drug proved effective as a hemostatic, the maximum shortening of the coagulation time occurring one hour after the injection.

The exact manner in which oxalic acid acts in shortening the coagulation time is not known. Schumann suggests that it acts as a catalyzer which assists the action of the calcium, platelets, and tissue fluids in forming thrombin. Page, Russell, and Rosenthal think that it changes the surface tension of the membrane of the platelets and brings about the liberation of thromboplastic material in this way.

AUDREY G. MORGAN M.D.

Boyer E. H., Flippin, H., Verwey W. F. and Woodward, R.: The Effect of Para-Aminohippuric Acid on the Plasma Concentration of Penicillin. *In* *Man. J. Am. J. Dis.* 1944, 126, 1007.

The authors note that when sodium para-aminohippurate and penicillin are administered simultaneously the former compound competes with penicillin for the same renal tubular excretory mechanism. By doing so the rate of renal elimination of penicillin is much reduced which slows up considerably the rate of fall of the plasma concentration of the antibiotic agent. A combination of these agents was administered continuously to experimental animals without the production of the functional or histomorphological changes attributable to the two agents. Moreover it was shown that the acute toxicity of sodium para-aminohippurate was very low.

In view of the implications of the possible therapeutic efficacy of the combination, it was decided to obtain data on a few patients to determine whether the simultaneous administration of para-aminohippuric acid with penicillin produced an elevated plasma concentration of the antibiotic agent. A careful study of the patients for any untoward reactions was thereby permitted. The methods followed in the administration of penicillin to 9 patients are presented. The methods for the plasma assays of penicillin and of para-aminohippuric acid also are presented.

The results of the tests on these 9 patients are summarized in a tabulation. Examination of the table reveals that in every instance the administration of para-aminohippuric acid with penicillin caused at least a twofold increase in plasma concentration of the antibiotic agent. There was a definite relationship between the plasma concentration of para-aminohippuric acid within this range and the amount to which the penicillin level was elevated. There was no outstanding difference in response due to age, sex, or race.

The pharmacodynamic effects of sodium para-aminohippurate are considered in two categories: (1) those attending the injection of the priming doses, and (2) those occurring during or following the para-aminohippuric acid infusions. Only when para-aminohippuric acid was administered at room temperature was any reaction noted. The only noteworthy untoward effect which occurred follow-

ing the administration of certain of the priming doses of para-aminohippuric acid was a contraction of the smooth musculature of the large intestine and bladder unattended by pain or discomfort. The infusion of para-aminohippuric acid and penicillin continuously for twelve hours produced no discernible deleterious effects on the patients who manifested a number of unrelated disease entities.

The authors suggest that the plasma concentration of para-aminohippuric acid be checked frequently to make sure that the function of diseased kidneys is sufficient to allow excretion of the drug rapidly enough to prevent an excessive blood level of para-aminohippuric acid. Moreover the authors note that more effective plasma concentrations of penicillin were found to be present in patients who had known renal involvement. In the light of recent work, this can be interpreted as being due to renal damage which decreases the transport capacity of the tubular excretory mechanism.

HERBERT F. THURSTON M.D.

Opazo, V. Retinal Hemorrhage following Transfusion (Hemorragia retiniana post transfusional). *Bolet. Soc. Chilena Obst. Gyn.*, 1944, 9, 153.

Attention was first called to the complication of retinal hemorrhage following blood transfusion by Sallmann in 1935. Since then a number of cases of retinal hemorrhage and one of permanent and one of temporary blindness following transfusion have been reported.

The author reports a case in a woman of forty-nine who was to be operated on for ovarian cyst after previous treatment to improve her general condition. The circulatory system was normal. She was given three blood transfusions, and about three and one-half hours after the third transfusion retinal hemorrhage developed.

After a discussion of the cases reported the author concludes that this complication occurs only when there are predisposing causes such as long-continued anemia, and that it occurs most frequently when repeated transfusions have been given. He believes it is not a serious complication, although some students of the subject think it is.

AUDREY G. MORGAN M.D.

Koop, C. E.: The Use of a Specially Prepared Gelatin Solution as a Plasma Substitute. *Surg. Clin. N. America*, 1944, 24, 1300.

Koop holds that gelatin is the best of the plasma substitutes and that it is equal to plasma in the treatment of shock. It is remarkably nontoxic and nonantigenic. The gelatin solutions used were specially prepared from selected raw materials to the finished product in a plant designed especially to prepare gelatin for intravenous administration to patients. Colloidal solutions such as gelatin are offered not as substitutes for whole blood but rather as substitutes for plasma. Plasma is used chiefly for its coagulating function, its nutritional value, its aid in the defense against infection, and for the proper

ties associated with the colloidal osmotic pressure of its proteins. Whole blood is used more extensively than plasma for its antihemorrhagic and antibacterial properties. The chief use for which plasma is employed is for the colloidal osmotic pressure of the plasma proteins when the desired result is maintenance of an adequate blood volume and its many related physiological phenomena. It is for this particular purpose that gelatin solutions are used so efficiently.

The criteria for an ideal plasma substitute are the following:

1. **Physical properties.** An ideal plasma substitute should be stable, of low viscosity and have a high colloidal osmotic pressure and the colloidal particle size should be sufficiently large to cause it to be retained in the circulation long enough to be effective. Finally there should be no difficult problems with storage.

2. **Physiological properties.** It must be safe for injection in large quantities, and it should not interfere with blood coagulation, the defense against infection or tissue repair. It must be nontoxic.

3. **Immunological properties.** It should not be an antigen and it should have no natural sensitivity to similar substances such as foods or sera.

The gelatin solution which has been most satisfactory is one prepared by hydrolysis of alkali treated long bone collagen under controlled and standardized conditions. It is administered as a 6 per cent solution in physiological saline solution after autoclaving for twenty minutes. (This is the solution Knox P so referred to by the National Research Council in its report on Gelatin as a Plasma Substitute. *J. Am. M. Ass.*, 1944 125: 284.) This solution is preferred for the treatment of shock because its method of preparation produces the optimum molecular size of the gelatin, upon which its physiological action largely depends.

When gelatin solutions are subjected to high temperatures, such as those required in sterilization by autoclave, the long gelatin aggregate molecule is broken down to form a larger number of smaller molecular particles. Whereas the smaller molecules theoretically exert a higher oncotic pressure, they are excreted from the blood stream through the kidneys so rapidly that their effective oncotic pressure is short-lived and not of the sustained value of the larger molecules which actually exert a lower osmotic pressure. For this reason two factors are of importance in the manufacture of gelatin solutions for plasma substitute: the source of the gelatin and the method of preparation of the solutions. Bovine long bones are a better source of gelatin than skins, hides, or fish products because of their relative freedom from bacterial and fungus contamination and their uniformity of composition. Gelatin solutions for intravenous use should be prepared for that purpose and apart from the commercial manufacture of edible gelatin. Even the use of pure U.S.P. edible gelatin in the preparation of intravenous solutions may result in a pyrogenic product because of im-

purities that may render it unfit for parenteral use. There are several advantages in the preparation or processing of gelatin solutions. Whereas the preparation of plasma must be undertaken with the most rigid sterile technique, gelatin solutions, if prepared with reasonable cleanliness, can be thoroughly sterilized in the last step of manufacture by autoclaving and Seitz filtration. Gelatin solutions need not be refrigerated as fresh plasma must be, and they can be kept in a single container as compared with the two needed for hypophilled plasma. When the solution is prepared as a single dose package, no preservative need be added. This avoids the possible danger of chemical phlebitis due to preservatives. The great advantage of gelatin is that it is readily available at relatively low cost and that we are not dependent upon blood donations to obtain it. This is of special practical importance in localities and hospitals where plasma banks are not established.

Gelatin solutions are miscible with all of the usual intravenous solutions and can be administered by means of any of the "open" or closed methods. The open system, which is frequently used for transfusions of whole blood or plasma, has been satisfactory for use with gelatin. Unless heated, gelatin solutions of the type recommended are in the physical state of a gel at ordinary room temperature in the temperate zone. However because the gelation point is lower than the melting point, these solutions, once warmed remain fluid at room temperature unless exposed to a cold atmosphere such as that from an open window. Gelatin solutions kept in a warm closet at 37°C. are ready for immediate use. Inasmuch as there is a very slow deterioration, or shortening of aggregate molecular chains, such solutions should not be stored at 37°C. over a month. An alternate method of preparation is immersion of the gelatin bottle in a hot water bath until melting takes place. Minimal viscosity and hence greater speed of infusion is found at 50°C. The return to the gel state does not occur until ample time has passed for administration at ordinary room temperature. As with plasma or whole blood, it is advisable not to use needles of a size smaller than 19 gauge for gelatin infusions. In the treatment of shock during which it is occasionally of advantage to administer gelatin relatively rapidly an 18-gauge needle should be used. It has not been necessary in the cases treated to infuse gelatin under pressure, although there is no reason why such a method would be impractical because of any properties of gelatin. It is possible to administer a suspension of erythrocytes with gelatin. This is an inexpensive procedure in those places where erythrocyte suspensions are available without cost as a by-product in the preparation of plasma. One difficulty arises in the administration of gelatin-erythrocyte suspensions. Gelatin increases the sedimentation rate of erythrocytes, and thereby occasionally causes the needle to become plugged by the high concentration of cells in the dependent portion of the apparatus if some precaution is not taken. The addition of a 5

per cent dextrose solution in equal quantity facilitates the administration of gelatin and erythrocytes. A more complicated but certain method is to bubble oxygen through the mixture to keep the cells in uniform suspension. The size and frequency of infusion must be governed by the requirements of any given case. Gelatin infusions must be given with the same care as an infusion of plasma and may be given for similar indications.

The administration of single and repeated infusions of ossein gelatin has been accompanied by few local or general reactions. Venous thrombosis has occurred in less than 3 per cent of infusions. This was true even when phenyl mercuric borate was added to the gelatin as a preservative. No unusual difficulty has been encountered in local extravasations of gelatin solution from its accidental introduction subcutaneously. The use of hot wet dressings is of advantage in hastening the absorption of such collections.

THE CLINICAL USE OF GELATIN SOLUTIONS

Treatment of shock Experience in treating shock following burns, hemorrhage and trauma has demonstrated gelatin solutions to be effective. It is difficult in clinical practice to judge the comparative efficacy of a plasma substitute, as one is separated from the controlled conditions of the laboratory. Studies on volunteers bled into shocklike states while under observation on the ballistocardiograph have established the efficacy of gelatin in the treatment of hemorrhage on physiological grounds. As a routine in the treatment of shock an intravenous infusion of 6 per cent gelatin is started as soon as possible. Usually 500 cc. are sufficient to bring about a rise in blood pressure and pulse volume but occasionally more are required. It may be desirable to give another gelatin infusion several hours later or to give a whole blood transfusion. The rate of infusion is important in some cases of shock. It is customary to administer the solution as rapidly as it will flow by gravity through an 18 or 19 gauge needle. In cases of hidden hemorrhage an effort should be made to keep the patient out of shock but to maintain his blood pressure at a sufficiently low level, usually about 100 mm. of mercury systolic, to favor clot formation and to discourage brisk bleeding. One possible danger of administering large quantities of gelatin to such patients is that they may continue to bleed internally but fail to show a fall in blood pressure or an elevation in pulse because of the maintenance of blood volume. The severe anemia which may develop is detected only by the observation of pallor or a marked fall in hemoglobin or hematocrit reading.

Treatment of burns Gelatin has been used to some extent in the treatment of burns, but E. I. Evans has treated a comparatively large series of second-degree burns with gelatin with success comparable to that obtained with plasma. He believes that repeated infusions of 500 cc. of gelatin solution every four to six hours is a better practice than less

frequent larger infusions, and that after thirty-six or forty-eight hours whole blood is usually indicated. Because of the size and shape of the gelatin molecule it is likely that it is lost less readily from the surface of a burn than is plasma, although no accurate data are available. The probability of this phenomenon serves as a reminder however that while the blood volume and hematocrit reading might be maintained the plasma protein can leak out of the denuded area to produce a severe depletion of natural serum proteins. With our present knowledge it would seem advisable to give whole blood or plasma to the patient treated with gelatin who survives the shock phase of his burn. The use of gelatin solutions intravenously in no way alters the use of adequate local treatment to the burned area.

As a supportive measure in operative surgery In a patient about to undergo surgery under serial spinal anesthesia, a gelatin infusion before or during the procedure has very frequently prevented the expected fall in blood pressure. Especially in emergency surgery under any type of anesthesia, the use of gelatin infusion during an operation has aided many patients in coming through an otherwise difficult procedure without the added danger of an unstable pulse and falling blood pressure. On several occasions during emergency surgery when gelatin solutions were used the response of the patient was impressive.

Treatment of edema It is in this field especially where little is known about gelatin, that there is need for further investigation. Gelatin solutions have been effective chiefly in edema due to hypoproteinemia which may itself be due to many causes. The author has been successful at times in treating edema due to starvation liver cirrhosis, and nephrosis as well as several cases of terminal anasarca in lymphosarcoma and Hodgkin's disease. In the management of these problems, daily infusions of 500 cc. or 1000 cc. of a 6 per cent gelatin solution were given, with a close watch on the serum albumin concentration. The use of mercupurin in doses of 2 cc. after several gelatin infusions has resulted in greater diuresis in certain cases than either mercupurin or gelatin solutions alone. Because of the increase in blood volume which follows gelatin infusions, its use should be avoided in patients with edema of cardiac origin. The large molecular gelatin produces greater diuresis than the small. In several instances, administration of the small molecular gelatin has been followed by an increase in weight. The gelatin concentration of edema fluid has been found to be greater after infusion with the small molecular material than with large molecular gelatin. We have been asked if gelatin has an effect on pleural effusions or abdominal ascites. No such hope was entertained and no beneficial effect has been seen, although peripheral edema associated with either of these conditions may be benefited.

The chief precaution to be observed in the use of gelatin solutions is one suggested by the circulatory

changes after gelatin infusion. The 6 per cent gelatin solution has twice the oncotic pressure of plasma and, therefore, must be used with caution in patients of doubtful cardiac status. It should not be used at all in patients with any signs of cardiac failure, no matter how slight. As it has been shown the maximum blood volume increase occurs three hours after infusion and for that reason cardiac decompensation may occur some hours after the close of an otherwise uneventful gelatin infusion. Paradoxically the availability and low cost of gelatin solutions are in themselves sources of potential danger for without need of blood donors or the necessary formality of obtaining plasma from the plasma bank, the clinician has a large supply of a powerful agent ready for immediate and continued use. If the limitations of gelatin solution are kept in mind and it is used with the same judgment and precaution as plasma and for similar indications, it will prove an effective plasma substitute.

BENJAMIN GOLDMAN, M.D.

RETICULOENDOTHELIAL SYSTEM

Fotheringham, W. T. and Sugasti, J. A.: The Importance of Roentgenology in the Diagnosis of Traumatic Ruptures of the Spleen (Importancia de la radiología en el diagnóstico de las rupturas traumáticas del bazo). *Rev. As. méd. argent.*, 1944, 58, 9, 3.

Traumatic ruptures of the spleen without an open wound of the abdomen are extremely rare. Only 8 have been seen among 3,500 admissions to the Emergency Surgical Service of the Public Welfare Hospital of Rosario.

Unless the hemorrhage is very profuse and floods the peritoneum at once there is generally a latent

period during which the clinical symptoms are slight and indefinite. It is during this period that diagnosis should be made in order that surgical treatment can be effective. The only means of making an absolutely certain diagnosis is by roentgen examination. If the possibility of rupture of the spleen is suggested by pain in the left hypochondrium irradiating to the shoulder of the same side a simple screen examination without contrast should first be made with the patient standing. This will show an abnormal opacity at the bed of the spleen which pushes the left diaphragm up and renders it immobile. The great tuberosity of the stomach is pushed toward the midline and the air chamber is reduced in size. The splenic angle of the colon is pushed downward and inward. An examination with contrast medium is then made which confirms the changes in the air chamber of the stomach and shows others in its middle part, a characteristic image.

The diagnosis can be confirmed absolutely by the injection of about 1,000 cc. of air followed by screen examination. This shows the spleen in the greatest detail, particularly its upper pole. Its base passes into an opacity which shows a fluid level extending from the lateral surface of the spleen to the ribs. Sometimes there are other fluid levels in the right hypochondrium. If the patient is moved slightly there is an unmistakable wave in the fluid level. These changes should be recorded on roentgenograms.

The authors describe 6 cases in which they made the diagnosis by means of roentgen examination and present the roentgenograms. In 3 other cases in which pain in the left hypochondrium suggested traumatic rupture of the spleen roentgen examination proved that it did not exist.

AUSTIN G. MORROW, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Moore, T : Underwater Blast Injuries of the Abdomen. *Brit. M J* 1944, 2 626

The basic mechanism of underwater blast injuries to the abdomen is still uncertain. This article is based on the treatment of 18 patients, 9 of whom were subjected to operation. There were also 22 other patients who were examined and questioned and kept under observation after having been operated upon elsewhere.

In underwater blasts there is no after wave of negative pressure, thus the abdomen is affected more than the thoracic cavity. The shock of the explosion on the abdomen may be described as being like a severe kick or a viselike tightening as though the abdominal contents were forced up through the body into the head or as if a giant hand were squeezing the body from the waist downward. Many victims have the sensation of having the legs shot away. Several patients have had temporary paraplegia. None of the patients in the group described complained of pain in the testes.

Following these painful symptoms the patients managed to swim but after they had been picked up by another vessel they found they could not straighten themselves up or walk because of abdominal pain. After rescue there may be an urgent desire to defecate a blood-containing stool. Vomiting is a very common symptom.

Clinically these patients show all the signs and symptoms of a generalized severe abdominal blow. Many die at once or shortly after their injuries from shock and hemorrhage. The clinical picture in those rescued varied according to the time which had elapsed since the injury, and the extent of the injury. The more severe the injury the more severe the abdominal pain, vomiting and shock.

The most important early factor in the diagnosis is to know whether intestinal perforation has occurred. The greatest attention must be paid to the local abdominal signs, the most important of which are tenderness and rigidity. Intestinal perforation may be stimulated by intraperitoneal hemorrhage and by injury to the lungs.

The author places great reliance on the observation that if rigidity is caused by peritonitis due to perforation the abdomen does not relax during expiration. Late perforations of the intestine may occur.

The most important lesions are hemorrhage and perforation. Hemorrhages may be of the scattered pinpoint type, the linear subperitoneal, or the massive, irregular subperitoneal type. Perforations were found in the ileum and in the ascending and pelvic colon. Perforations varied from the size of a pin point to 3 cm. in diameter. Frequently there is only one perforation but at times several may be found.

Various other hemorrhages and injuries to the internal organs are described. Gas-containing abdominal viscera are most commonly and markedly affected.

Any one within 200 yards of the explosion is in danger and those facing the explosion are usually more seriously injured than those with their backs to it. Distance is the best safeguard against injury and the safest position appears to be floating on the back.

Treatment consists of rest, warmth, morphine and intravenous infusions of blood or plasma. Mask administration of oxygen is used for patients with chest lesions.

Late perforation must always be considered and appropriate measures taken. In cases of perforation operation is performed as soon as the patient is fit for surgery. Spinal analgesia is suitable if shock has been overcome. Intravenous administration of pentothal sodium combined with local block are useful in these cases. One of the sulfonamides is used before the abdomen is closed. Ordinary suture of the colon is carried out and the peritoneal cavity is drained. Continuous gastric aspiration and the intravenous administration of fluid and sulfonamides are extremely important postoperatively.

Nine of the 18 personal cases were submitted to operation. Perforations were found in 8 of the patients. There were 2 deaths and in these cases perforations of the intestinal tract and blast lung were found. The mortality among the operative cases was 22 per cent.

The postoperative complications were peritonitis, purulent bronchitis and acute obstruction of the small intestine. Two of the patients who had been treated elsewhere previously for perforation of the bowel, subsequently developed intraperitoneal abscess. Another patient developed a subphrenic abscess.

RICHARD J. BENNETT JR., M.D.

Mitchell, G. A. G. : Infection in War Wounds. *J. R. Army M. Corps* 1944, 85 225

Mitchell attributes the high incidence of infected wounds in military as compared with civilian life to (1) the severity of the average battle wound, (2) the proportion of open or closed fractures and joint injuries, and the degree of bone and soft tissue damage, (3) the soiled character of the soldier's skin and clothing, (4) penetration and perforation of the body cavities, (5) the presence of foreign bodies and their irritant nature, (6) the circumstance of exposure to excessive heat or cold, battle strains, and lack of food and drink, (7) the circumstance of immediate treatment on the battlefield, (8) the necessity of transporting many hundreds of miles over difficult country before the wounded reach hospitals, and delays in getting definitive treatment, (9) the difficulty of maintenance of strict asepsis under battlefield

conditions, and the risk of cross infection and (10) infection from vectors such as flies.

Bacterial infection was of the mixed type in all except 6 of the cases observed the most common combined infection being caused by streptococci and staphylococci, although other organisms were often present with these in the same wound.

Streptococcal infections usually proved more troublesome in the earlier stages and were more liable to produce signs of general intoxication, while staphylococci were more persistent and difficult to eradicate, and were present in a high proportion of the truly chronic wounds.

The bacteriologist can provide invaluable help yet too much emphasis must not be laid on the laboratory findings and prevent definitive treatment.

The cautious assessment of laboratory reports is especially necessary when the clostridia group are considered. In the orthopedic cases, these organisms were present in 25 per cent of the wounds, but only 1 patient had true gas gangrene and he might have escaped this complication if his grossly lacerated and contaminated leg had not been encased in an unsplit, unpadded plaster with consequent swelling and interference with the circulation. The presence of clostridia organisms should never by itself lead to a diagnosis of gas gangrene. The diagnosis can be made with certainty only on the clinical appearance and examination of excised portions of the affected muscle.

Infected war wounds, like any others, may become chronic. Every general hospital with many casualties always has its quota of chronic cases. Figures show that approximately 33 per cent of the wounds at the author's hospital were still unhealed after two months, but in three months the number had fallen to 10 per cent largely because the removal of sequestra in 7 cases led to healing of persistent sinuses. The wounds slowest to heal were the sequel of mine explosions, and most of those were heavily contaminated and contained multiple foreign bodies.

The causes of chronicity in war wounds are many and various, but possibly the two chief ones are the gross and extensive nature of the original injury and the fact that infection is often well established before the surgeon has a chance to prevent it.

There are other factors also. The area of skin loss may be so great that healing by natural processes must inevitably be a lengthy process. The patient may be debilitated and his resistance undermined by strain, exhaustion, loss of blood, or a virulent infection. He may have suffered from lack of proper food and water, and in a few cases there may be some constitutional disease, such as nephritis, which reacts unfavorably on the reparative powers.

STEPHEN A. ZIDMAN, M.D.

Neel, H. B., and Cole, J. P.: Gas Gangrene in Amphibious Warfare in the Pacific Area. *Am J Surg* 94:4, 66-90.

In 984 consecutive fresh battle casualties there were 7 cases of gas gangrene. In all the cases a

gram-positive bacillus, morphologically and culturally identified as the clostridium welchii, was found. The incubation period varied from one and one half to five days. The average time that elapsed between the injury and the appearance of the symptoms was two and thirty five hundredths days.

The lower extremity was the site of the infection in 5 cases, and the upper extremity was involved in 2 cases. The wound in each case was large, deep, and irregular and it involved muscle. In 5 cases, fractures were present, and in 1 case amputation had been done previously.

In nearly all of the cases, pain was the initial symptom. Two patients were delirious on admission to the hospital. Local swelling, discoloration, crepitus, and a foul odor are the early diagnostic signs. Evidence of toxicity appears late in the course of the disease. A persistent elevation of the pulse rate was present. The temperature was not a reliable index to the severity and extent of the infectious process. A low erythrocyte count and a low hemoglobin content were the most striking laboratory findings. In 1 case the diagnosis was confirmed by x-ray examination.

The treatment, both prophylactic and therapeutic, is primarily surgical. Early care of wounds and excision of devitalized tissue may reduce the incidence of gas gangrene. In 1 case excision of the wound gave satisfactory results. In the remaining 6 cases, amputation was necessary. Wounds should be left open, and vaseline gauze should be placed in them. Spraying of the stump with microcrystalline sulfathiazole was the practice in the hospital ship.

In patients with wounds of the extremities which are obscured by casts, early diagnosis of gas gangrene is difficult. The patient should be questioned frequently concerning the presence of pain. The cast should be examined for the characteristic odor of gas gangrene swelling below the cast should arouse suspicion.

Multiple transfusions of whole blood were found to be the most valuable single adjunct to surgery.

Two of the 7 patients died.

SAMUEL KARR, M.D.

Hutchinson, D. F. and Chapman, H. R.: The Evacuation of Casualties from a Normandy Beach. *J R Army M Corps* 94:4, 83-90.

This article narrates in detail the plan employed in the evacuation, transportation, and disposition of casualties from the Normandy beaches during the initial stages of the invasion assault. This consisted in evacuation of all casualties by sea from each of the 3 British sectors. An organization known as the Casualty Evacuation Point was set up on or near to the beach. It collected the casualties in D.U.K.W.'s (ducks), and transported them to Landing Ship Tanks (LST) anchored at sea.

On D+1 day the LST was beached and the casualties were loaded aboard after the ship had discharged its cargo of men and supplies. Sixty per cent of the casualties were evacuated in this manner.

each LST accommodated 144 bed patients and walking patients and evacuation fell into 2 categories according to the water tide—the low tide, when loading was done directly onto an LST and the high tide, when it was done onto a hospital ship anchored from 3 to 5 miles out from shore on the carrier's water ambulance or a Landing Ship Tank from a harbor 2 miles from the CEP. Every patient sent to the Casualty Evacuation Station was seen by a medical officer on arrival, was given a meal or some tea, had his dressings adjusted and was given whatever adjustment treatment might be required, also cigarettes and sweets. Here he could rest until evacuation was feasible, during which time his documents were checked.

The activity which received these patients was well organized: there were 3 medical officers in the Reception Center on duty during the day and night.

STEPHEN A. ZILMAN, M.D.

Gray R. O. and Mossendow N. A.: *Embarkation of Casualties from a Beach Head*. *J R Army Med Corps* 1944 83 215

This article discussed the evacuation of casualties from a beach-head, describing in detail the various methods employed. The plan of evacuation consists in using a Casualty Embarkation Point on the beach which collects the casualties and disposes of them principally by dispatching them to hospital craft. There are 2 types, the hospital ships and the hospital carriers. The latter are smaller and intended for short voyages only; consequently they have a specialized staff than the hospital ships. Each of the vessels serve several beach sectors and are supplied by Landing Ship Tanks (LST) water ambulances (usually 6 in number) from the hospital ship (LST), Landing Craft Tanks (LCT) with a capacity of 100 stretchers and 100 sitting patients, Landing Ship Infantry (LSI) with a capacity of 40 stretcher and 60 sitting patients, motor launches carrying 14 stretcher and 30 sitting patients, and DUKWs, which amphibious craft carrying 9 stretcher patients. When landing strips could be established evacuation by air was also employed; however certain serious patients for whom air travel was considered were denied this form of transportation. These were patients suffering from shock, abdominal and thoracic wounds, acute abdominal conditions, severe hemorrhage (including hemoptysis and atelectasis), gas gangrene, chemical gases, lobar pneumonia, pneumothorax, angina pectoris, coronary occlusion (during first month of condition) and lengths (during period of increased intracranial pressure).

STEPHEN A. ZILMAN, M.D.

Gray J. H.: *Reception and Evacuation: Notes on Administrative Problems Arising in a Large General Hospital (1,500 Beds) Acting as a Casualty Clearing Station*. *J R Army Med Corps* 1944 83 220.

This article describes the administrative problems which arose during the time in which the unit in

question functioned as a general hospital although its staff was limited to that of a casualty-clearing station. The clerical staff worked in a twelve hour shifts although these were stretched on many occasions to shifts of fourteen or fifteen hours duration.

The cases were received in a Reception Tent where documentation, sorting of patients, and exchanges of equipment were done. A convoy of 200 could be cleared in this manner within two hours.

After the convoy had been admitted the index cards were sorted and filed alphabetically.

When a patient was ready for evacuation a form was filled out; urgent cases were indicated with a priority label, also those requiring special handling, such as air patients and those with maxillofacial and head injuries. Clean x-ray films were included among the transporting records. The patients were then placed on evacuation vehicles, motor car or train ambulances, planes, or other conveyances, at which time all items were checked.

This system of recording by index cards has proved of inestimable value and was arrived at through trial and error. It has been modified according to circumstances but its value is worth the extra trouble entailed.

STEPHEN A. ZILMAN, M.D.

OPERATIVE SURGERY AND TECHNIQUE POSTOPERATIVE TREATMENT

Hamilton H. H., Custer B. S. and Kellner A.: *Pilonidal Cyst; An Analysis of 132 Consecutive Cases*. *Y England J Med* 1944 231 757

This analysis of 132 cases of pilonidal cyst calls attention to a method of preoperative grading which proved helpful in determining those cases suitable for primary closure. The preoperative classification of cases was as follows:

Grade 1: On examination the patient presents a sinus or sinuses and a palpable tumor but there is no history of inflammation or discharge.

Grade 2: The patient presents a history of discharge and recurrent local tenderness and swelling but not within the eight weeks prior to examination.

Grade 3: The patient presents a history of recurrent discharge or previous abscess formation requiring drainage.

Grade 4: The patient presents acute suppuration and abscess formation.

The series was thus divided as: grade 1, 45 cases; grade 2, 24 cases; grade 3, 45 cases; grade 4, 9 cases; and ungraded, 9 cases, of which 4 did not come to surgery and the remaining 5 were treated by excision and packing.

Excision and primary closure were done in 43 grade 1 cases, with 1 failure (2 per cent); in 20 grade 2 cases, with 3 failures (15 per cent); in 19 grade 3 cases, with 10 failures (53 per cent), and in none of the grade 4 cases. Failure is defined as any primary closure that requires reopening or that on follow up examination shows tissue breakdown or evidence of recurrence. The procedure of Ferguson and McCreay with minor modifications was followed.

In 82 cases treated by primary closure including the failures, the average time from operation to return to duty was twenty five days. Excision and packing was done in 24 of the first 66 cases, and the average time of hospitalization was sixty two days. Only 4 of the remaining 62 cases received this type of management, and the period of hospitalization averaged one hundred and two days. This procedure has been supplanted almost entirely by that of partial closure.

The technique of partial closure used by these authors was that of MacFee. This type of management was used in 21 cases, in 9 of which the cysts were of grade 3, in 1 the cyst was of grade 4, and in 1 of grade 1, this cyst being too large for complete closure. The average period of time from operation to return of the patient to duty was forty five days.

The procedure of incision and drainage was limited to 7 cases of gross suppuration and abscess formation. Incision and drainage at the outset and careful use of cauterizing agents effects a cure in simple types of abscesses. Care is taken to excise the fistulous tracts at the time of operation, and the wound is loosely packed with sulfanilamide gauze for one week. After this, the wound is treated daily with Carnoy's solution and saline solution until a clean granulating surface is presented. These patients were discharged to duty as healed in an average of twenty-seven days after operation.

It is concluded that grade 1 and grade 2 cysts may be satisfactorily closed by the modified Ferguson technique, with only rare failures and recurrences. Grade 3 cysts should not be closed primarily since failure occurred in 53 per cent in the cases so treated. The average hospital stay of the 128 patients operated upon for all grades of pilonidal cyst (from date of operation to complete healing and return to duty) was thirty five days. JONES L. LUDGIST M.D.

Karpovich, P. V., Starr, M. P., and Weiss, R. A.: Physical Fitness Tests for Convalescents. *J. Am. Med. Ass.*, 1944, 76: 873.

From an analysis of data presented it was found that three days after an acute fever of two and a half days duration an IAF cadet can pass a physical fitness test equivalent to walking up to a height of 20 feet and down again in thirty seconds (approximately to the third floor of an average building). One and a half additional days after fever the convalescent cadet can pass a physical fitness test equivalent to climbing up 100 feet and coming down in five minutes (approximately to the twenty first floor). After three more days he can make a score of 75 on the Harvard test for discharge to full military duty. The use of the Harvard test score of 75 is reliable for discharge to full duty since all of 271 cadets were able to carry on without relapse. Testing and participation in the physical training of the convalescent training program reduced hospitalization somewhat, definitely did not prolong illness, and insured adequate physical fitness for return to full military duty. From a small number of cases results

suggest that sedimentation rate (Westergren method) of the order of 24 to 35 mm. is not a contraindication to full participation in the hospital physical training program.

The clinical physical tests described in this article were used to assist medical officers in classifying IAF cadets convalescing from acute uncomplicated upper respiratory diseases for participation in a gradual physical training program. Participation in the physical training program resulted in a sufficiently high degree of physical fitness for the return of the subjects directly to full military duty when discharged from the hospital. J. M. MOON, M.D.

Brunschwig, A. and Nichols, S.: The Retention of Intravenously Infused Gelatin. *Surgery* 1944, 16: 9-13.

In recent years parenteral injection of nitrogenous nutriment has become feasible by virtue of the development of casein digests suitable for intravenous injection. Evidence has also been presented in support of the view that protein molecules (homologous plasma proteins) injected intravenously might be utilized for nutrition. The use of "complete" foreign proteins would not seem possible in view of their antigenic properties. However certain samples of gelatin have recently been found to be suitable for intravenous injection in that after their administration no immediate reactions were produced (except in isolated instances and these were not serious), sensitization did not develop and no later toxic effects were manifested. Gelatin, however, is an incomplete protein in that it lacks a number of the essential amino acids. As the sole source of protein in the diet it will not permit normal growth and development of experimental animals.

In view of the tolerance of human patients to repeated intravenous injections of gelatin and evidence that some of it is metabolized studies were carried out by the authors in a series of 23 patients to determine how much of this material is excreted in the urine under the usual conditions of intravenous clinical administration. This question is of obvious importance because if most of the injected material is excreted unchanged in the urine, little opportunity for utilization will be afforded.

Twenty three patients with various conditions received one or repeated daily intravenous injections of gelatin. In some instances the injections were made in the immediate postoperative period and the studies were carried out when the patient was receiving almost nothing by mouth. In others, the studies were carried out while the patient was partaking of the usual hospital diet.

As a result of their observations the authors present evidence to indicate that from 40 to 43 per cent of the gelatin injected intravenously in man as an 8 per cent solution in physiological saline solution is retained, as only from 60 to 57 per cent is recovered in the urine. The relative amount of gelatin retained is approximately the same whether 1 or 5 daily injections are made. Thus, the intravenous

Injection of gelatin constitutes one method by which antigenous material may be administered to the organism.

It is not to be inferred that these studies are regarded as final evidence to justify the assumption that gelatin given intravenously is a protein food. Evidence of appreciable utilization has not yet been presented. Emphasis is placed only on the fact that protein in the form of gelatin may be administered to the organism with the retention of appreciable quantities of the gelatin by the organism.

JOSEPH K. NARAY M.D.

ANTISEPTIC SURGERY TREATMENT OF WOUNDS AND INFECTIONS

Fleming, A., Young, M. Y., Suchet J. and Rowe, A. J. E.: The Penicillin Content of the Blood Serum after Various Doses of Penicillin Given by Various Routes. *Lancet* Lond., 1944, 247: 681

Penicillin appears in the blood within a few minutes after an intramuscular or subcutaneous injection. From the point of view of getting the drug into the circulation, therefore, there is little to be gained by intravenous administration. Also the rapid rate of its disappearance from the blood is not markedly altered, whether the injections are given intravenously or intramuscularly.

The time at which measurable penicillin disappears from the blood is somewhat as follows:

Intramuscular dose	Time of disappearance
15,000 units.	2 to 3
30,000 units.	3
15,000 units.	4
30,000 units.	4 to 5
100,000 units.	5 to 6

The maximum titer obtained in the blood after the injection of 15,000 units is necessarily much less than after the injection of 100,000 units; therefore if the interval between injections is the same the larger the dose the higher will be the average penicillin content of the blood. When single injections are used, however, a continuous bacteriostatic power can be obtained in the blood much more economically by the use of smaller doses. Six doses of 15,000 units given every two hours will certainly maintain a bacteriostatic power in the blood for twelve hours, whereas 100,000 units in a single dose will last only from five to six hours. However, there are times when injections cannot be given frequently in such cases, the larger dose and less frequent injection are advantageous. There are times also when it is desirable to have a high concentration in the blood for only a few hours. If, for example, it is necessary to operate through septic tissues, a dose of 100,000 units given fifteen minutes before operation provides a high penicillin content throughout the operation and for an hour or two afterward, which seems to prevent any generalization or spread of the infection.

In hospitals, the most economical method of administering penicillin is by the continuous intramus-

cular drip. Even with a dosage of 60,000 units in twenty-four hours the blood serum is rendered bacteriostatic, and with increased dosage it becomes much more highly bacteriostatic.

As yet, no decision can be made as to whether it is better to maintain a constant low level of penicillin in the blood or to have a very high level for a short time after an injection, followed by a period of very low level before the next injection. Clinically both systems work excellently.

SAMUEL KAHN, M.D.

Myers, R. S., Aldrich, R. H., Howard, R. W., and Walsh, R. A.: The Use of Gauze Inoculated with *Penicillium Notatum* or Impregnated with Crude Penicillin in the Treatment of Surface Infections. *N. England J. M.*, 1944, 231: 761

In order to evaluate the use of gauze inoculated with *penicillium notatum* pieces of 28-by 24 mesh absorbent gauze were folded to form eight thick masses, cut circularly placed in clean Petri dishes and sterilized in a hot air oven for one hour at a temperature of 400° F. Five hundred cubic centimeters of distilled water were placed in an Erlenmeyer flask, to which was added 6 gm. of dehydrated yeast and 12 cc. of glycine. A separate mixture of 12 gm. of lactose, 12 gm. of cornstarch, and 30 cc. of cold distilled water was added. The contents of the flask was stirred well, and boiled for twenty minutes over a low flame. The Petri dishes and culture medium were cooled, and about 60 cc. of the medium were poured into each dish. A bit of the stock culture of *penicillium notatum* was then transferred to the plate with a flamed platinum loop. The dishes were placed in an incubator at a temperature of 23° C. The penicillin secreted during the growth process was deposited on the under surface of the gauze. Its concentration reached a maximum in twelve days and then rapidly retrogressed.

The plates containing the impregnated gauze maintained their potency for about two weeks when kept at a temperature of 5° C. or lower, and the crude penicillin liquor could be kept for about four weeks at a temperature of 5° C. without any appreciable loss in titer.

All cultures were insured against contamination. Before the dressings were applied the lesions were prepared by cleansing them with an aqueous cationic detergent or with hydrogen peroxide. Gauze pads inoculated with mold or impregnated with crude penicillin liquor were then applied and held in place by adhesive tape or bandages.

Several cases of uterine cervicitis were treated also. In these, a pad of the mold inoculated gauze or of gauze impregnated with crude penicillin was applied directly to the cervix. The dressing was held in place by a vaginal tampon for a period of thirty-six hours. With the exception of those on the uterine cervix, the dressings were renewed at intervals varying from one to four days. All of the patients were ambulatory which made it difficult to change the dressings more frequently.

Forty seven cases of surface infection were treated. Healing occurred in 25 and improvement was noted in 13 during treatment. The types of cases included leg ulcer chronic endocervicitis pilonidal sinus wound, mastectomy wound carbuncle burn of the neck, peroneal wound, and ulcerative stomatitis.

Chronic or mixed infections did not respond so well as did acute infections, or infections of but one strain of a penicillin sensitive organism.

Because of the difficulties associated with the preparation of crude penicillin and mold inoculated gauze, the authors advise that only purified penicillin should be employed for the treatment of cases of surface infection.

STEFAN A. ZIMAN, M.D.

Fauley, G. B., Duggan, T. L., Stormont, R. T., and Pfeiffer, C. C.: The Use of Penicillin in the Treatment of Peritonitis. *J Am M Ass* 1944 76: 13

Since peritonitis causes 92 per cent of all deaths in hospital patients admitted with a diagnosis of acute appendicitis, and it is also a frequent cause of death in ruptured peptic ulcer and penetrating abdominal wounds, the authors have prepared a controlled experimental study to ascertain the effectiveness of penicillin administration in controlling fulminating diffuse peritonitis.

They produced peritonitis in dogs by occluding the blood supply of the appendix by means of ligation of the mesenteric vessels and also of the base of the appendix and then giving 50 cc. of castor oil with the stomach tube. This type of peritonitis, with a bacteriological flora quite similar to peritonitis in man, has a mortality of approximately 100 per cent.

The authors picked dogs at random and divided them into three groups. The first served as a control. The second group, given the same supportive therapy as the first, was also given intramuscular penicillin therapy beginning one hour postoperatively and continuing every four hours until recovery ensued. The third group was treated similarly except that the penicillin therapy was not started until twenty-four hours after operation.

The clinical symptoms following the induced gangrene of the appendix in the dog are similar to those observed in appendicitis in man. In the control group 25 of 27 dogs (92.6 per cent) died of fulminating diffuse peritonitis in an average of fifty-seven hours. In the second group (penicillin starting one hour postoperatively) all 20 animals survived and at autopsy on the twenty-first day after operation no evidence of generalized peritonitis was present. The dosages used were 100 Oxford units per pound given intramuscularly every four hours to the first 3 dogs. Because of their critical clinical condition the rest of these animals received 150 Oxford units per pound every four hours for the first thirty-six or forty hours, then the dose was decreased to 5,000 units every four hours for two or three days, then to a total of 5,000 units every eight hours for two or three days. Twenty-eight dogs which developed the

operative complication of an internal fecal fistula died under penicillin therapy and were not included in these figures.

In order to ascertain the effectiveness of penicillin after the infection was well established, in the third group treatment was delayed until twelve hours after operation when definite abdominal rigidity was present. Penicillin was given as outlined for the second group with the result that 4 of 19 animals died a mortality of 21 per cent. The authors believe that large initial doses of penicillin possibly could have prevented these deaths.

The authors believe that since adequate penicillin doses given early are remarkably effective in the control of experimental peritonitis in dogs, it is reasonable to assume that the similar peritonitis in man due to appendiceal rupture will be favorably affected by adequate penicillin therapy. The longer the penicillin therapy is delayed the less favorable the results will be and the larger the dosages should be. Since relatively large doses of penicillin with regard to the body weight were used in these experiments, the authors believe that initial doses of 22,500 units per hour or about one-half million units per day would be necessary for a man weighing 150 pounds. As no toxic symptoms were displayed in this experiment and no serious symptoms have been described after massive doses in man, it would appear that large doses of penicillin are innocuous especially in relation to the critical nature of fulminating diffuse peritonitis.

In acute appendicitis the authors do not consider penicillin a substitute for early surgery based on sound surgical judgment, but they believe that its use may be indicated in such instances as (a) operations in which peritonitis is encountered or localized abscesses have been broken into, (b) operations on the large bowel or intestines when some sepsis occurs, (c) following gunshot or traumatic injuries to the abdomen, or (d) aboard small ships or submarines and at isolated posts where adequate surgery is not available.

ROBERT BLASLOW, M.D.

Burnett, W. E., Rosemond, G. P. and Caswell, H. T.: The Use of the "Sump Drain in Peritoneal Infection. *Surg Clin. America*, 1944 24: 36

The objectives of surgical drainage are as follows:

1. To remove exudate which may contain harmful toxins, necrotic tissue or living bacteria, or may cause mechanical interference with physiologic functions.

2. To allow ventilation and/or irrigation for combating anaerobes.

3. To produce by adhesions a limited space through which infectious material can be channeled at a subsequent time.

4. To indicate the type of exudate (blood, bile and so forth) from a hidden source.

5. To avoid the accumulation of exudate in an unavoidable or potential dead space (in amputations of the breast, extremities).

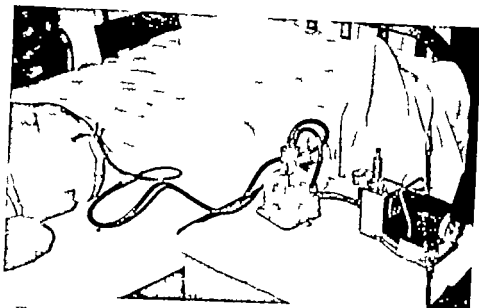


Fig. 1. A sump drain being used in generalized peritonitis. Note the exudate present in the bottle which has accumulated in eight hours. The abdominal dressing has not been changed in three days and is practically unsoiled. In actual practice the bottle and motor are on the floor.

Although only vaguely suspected at first, these principles have influenced doctors to utilize drainage for peritonitis since the infancy of surgery. Unfortunately the same protective process of adherence and loculation which surrounds and incarcerates contaminated areas tends to defeat drainage by walling off into many compartments the irritated peritoneal cavity. Thus, a drain consisting of an irritant foreign material was even more quickly sealed off from the remainder of the cavity often in a few hours.

Drainage in peritonitis is helpful in proportion to its efficiency. Gauze wicks tend to block drainage unless the exudate is thin, and cause early firm adhesions. Rubber of various compositions, is irritant and similarly is soon isolated. Drainage with such materials is of short duration; profuse amounts of exudate appearing for only a few hours. This has led to the search for less irritant materials which will not cause such rapid isolation.

In 1936 W. W. Babcock began seeking a drain of less irritant character which would increase the efficiency of drainage, more nearly approach the theoretical objective of the method and would be less likely to cause dense insulating adhesions. First glass, and later stainless steel fenestrated tubes were tried alone without gauze or other material about them. Inside each was a proportionately smaller tube, rubber at first, then stainless steel, connected to a motor-driven pump for constant aspiration of the pus which accumulated in these larger tubes, on the principle of a sump and this name was adopted for them.

In the treatment of peritonitis large quantities of exudate were withdrawn by this method in spite of operative aspiration. As much as from 100 to 200 cc. in each twenty-four hours for the first day or two has

been recorded. Often fairly large amounts continue for three or four days. Instead of becoming thicker and more malodorous, as seen with older types of drains, the material soon changes from purulent to serous, the odor disappears with varying rapidity and the serous fluid quickly diminishes in volume. This indicates absence of isolation and continued procurement of exudate as it forms. On several occasions the drains have been removed in two or three days because the patient's condition was excellent, peristalsis had returned, the graphic sheet was practically normal and only a little serous drainage was obtainable.

In addition to the important factors of decreased mortality and morbidity according to the authors tabulated experience in 96 cases other advantages of sump drainage are:

- 1 Removal of pus by positive means from the bottom of cavities instead of puddling and overflow from accumulation and body or intestinal movements as obtains with other methods. Thus even large but localized abscesses are more rapidly healed.

- 2 Frequent change of the small dressing is usually not required.

- 3 Ventilation and more adequate drainage decreases odor which is an important esthetic factor to many patients.

- 4 Pus is collected in a bottle with or without deodorant or antiseptic for easy disposal instead of on the dressings, clothing, and bedding for general contamination of the patient and attendants.

- 5 Postoperative hernia is much less likely — 1 or 2 small hernias were discovered at reoperation for appendectomy although they were not demonstrable before incision.

- 6 Postoperative obstruction is less likely. Two of the 62 patients, or 3.2 per cent, were submitted to

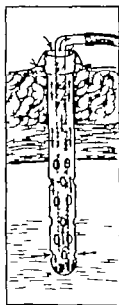


Fig. 2. Diagram of the sump drain. Note impossibility of direct suction on bowel or omentum provided there is a free airway between the inner and outer tubes. Note fish-mouth end of inner tube to avoid sealing.

ileostomy on the fifth postoperative day because of continued marked distention, but both had remained very septic and febrile, and the one on whom an additional blood count was taken showed continued leucocytosis. Both cases were interpreted as inflammatory rather than obstructive ileus, and both patients slowly recovered after ileostomy. Even when the condition is construed as being mechanical obstruction, its occurrence in 3.3 per cent of the cases compares favorably with the quoted statistics of 10 per cent and 7.4 per cent.

7 Postoperative secondary abscesses are rare. The one peritoneal abscess medial to the incision and two pelvic abscesses observed in these 62 patients occurred before the location of the drain was changed from right lower quadrant to the depths of the pelvis. Since this change, there has been no pelvic abscess formation.

In the extremely ill patients with diffuse peritonitis, shock is treated with plasma, blood, fluids, and adrenocortin. Without removal of the patient from bed an anesthetic is injected in the right lower quadrant for a 3-cm. muscle-splitting incision. Through this a long sump drain is gently inserted into the pelvis, being guided into the cul-de-sac by a finger inserted into the rectum. The sterile assistant can then anchor the drain to the skin with wire suture. No other sutures are needed. A modified Ochsen treatment including constant gastric or intestinal suction fluids, nutrition and blood (given parenterally) is applied. Sulfonamides may be used systemically or omitted. Appendectomy can be done when the patient has recovered sufficiently but not less than a week should elapse. For the average moder-

ately ill patient, appendectomy is done under spinal anesthesia through a small muscle-splitting incision. Pus which can be reached without trauma is removed by aspiration. A sump drain is inserted into the pelvis to drain it and the right lower quadrant. Powdered sulfonamides may be applied and the wound is closed about the drain in layers with fine steel sutures. The drain is anchored to the skin with No. 32 wire and modified Ochsen treatment is used.

The drains themselves vary greatly in size both as to length and diameter and in the size of the perforations in the outer tube. The larger-sized perforations are more satisfactory for thick exudate. The smaller perforations are suitable in cases with a thin watery exudate, particularly one composed of or containing bile. Perforations larger than 2 mm. may allow the entrance of omental tabs or even intestinal wall. In the photograph it can be noted that the drain protrudes a short distance above the skin level, even when dressings are applied. A thin dry gauze pad and a small aluminum cage is applied about this protruding portion which protects it from displacement by the bedclothes and from contamination, but does not interfere with the free passage of air down the outer tube as illustrated in the drawing.

Once the "sump set-up," consisting of drain, bottle, and motor is connected its care is quite simple. It is important to check the components of the unit for efficiency before it can be considered effectual. By clamping the tube to the motor and observing the rapid rise of the pressure gauge, one proves pump efficiency. By clamping the tube between the drain and the bottle the important fact that the bottle is air-tight can be determined by a steady rise of the vacuum gauge to the limit. Next the patency of the inner tube is checked by sudden release of this block. A characteristic sump suck and gurgle is heard as the built-up vacuum is opened to the abdominal portion of the drain. When there is abundant drainage the glass adaptor tube and bottle give visual evidence of function.

The most common difficulty encountered, namely blocking of the inner tube by exudate, frequently can be discovered by simply walking by the patient's bed. The block results in a progressive vacuum, and the motor can be heard laboring to maintain the level. Further examination will show the vacuum gauge to have risen above zero, and the blocking off of the tube from drain to bottle with sudden release does not result in the characteristic suck and gurgle. This difficulty can be readily solved by removing and cleaning the inner tube or by inserting a new one. When the perforations of the outer tube become blocked due to drying and crusting of the slight residual exudate, it is usually time for the drain to be removed. However if exudate is still present in the peritoneal cavity an applicator soaked with peroxide and swabbed about vigorously within the tube often results in dissolution of these obstructing crusts, and further drainage may occur.

Removal of the drain is a welcome contrast to the usually difficult and often traumatic removal of

gauge and rubber drains. In most cases cutting of the wire suture and a gentle, steady pull result in a painless removal with no bleeding. On occasion omentum may enter the perforations and cause some drag with pain. Rotation of the drain will release these attachments. The small aperture in the incision decreases considerably on removal of the drain, and the tract remaining lends itself readily to catheter drainage for progressive shortening to avoid pocketing. In several patients whose drainage was never profuse or odorous, this step has been omitted.

The steel sump drain lends itself most readily to cleansing and sterilization. Sterile sets of these drains are kept in the operating room at all times for selection when needed. They are most durable and last for indefinite periods with a minimum of care. Any standard noiseless continuous suction motor is efficient.

The principles of the sump drainage technique are most important:

1. The drain is made of stainless steel and causes no demonstrable irritation to tissue.
2. It should be placed into the most dependent part of the infected cavity. The patient's position should promote gravity drainage of exudate into this dependent area.

3. Only liquid exudate is subjected to the vacuum. No direct suction is made at any time against bowel, omentum or soft tissue unless dressings are erroneously allowed to seal the protruding end of the large tube. It is essential for proper functioning of the drain that there be free access of air and that there be sufficient space between the inner aspirating tube and the outer collecting tube to allow for its passage or else a vacuum against the bowel and omentum will occur.

4. Simple tests should be made frequently to insure proper function of the drain, bottle, and motor. If the vacuum gauge rises above zero there is blockage.

BENJAMIN GOLDMAN M.D.

ANESTHESIA

Cooper, W. G., II; Zumwalt, W., and Sugerbaker, E. D.: A Limited Comparison of Continuous Spinal and General Ether Anesthesia. *Surgery* 1944, 16: 886.

A comparison is made of 100 consecutive patients receiving general ether anesthesia and 100 consecutive patients receiving continuous spinal anesthesia. One anesthetist gave all of the ether anesthetics and another gave all of the spinal anesthetics. The patients were essentially similar in both series being indigent patients suffering from cancer with an average age of about sixty years and with many associated diseases other than the kind for which they were being operated upon. The relative consistency of all factors in both series with the exception of the type of anesthetic used made these series unusually good for comparative purposes.

It was noted that 44 per cent of the patients given ether anesthesia and 77 per cent of those given con-

tinuous spinal anesthesia were considered to have had satisfactory operative and postoperative courses. The incidence of hypotension was less in the spinal anesthesia cases and the occurrence of 3 fatal pulmonary emboli in the general-ether group alone seemed significant to the authors, who believed that the less complete relaxation produced by ether probably necessitated greater operative trauma. The technique of the continuous spinal anesthesia was described in detail. Routinely, a catheter was placed in the urinary bladder throughout the entire course of surgery. A stomach tube was inserted in patients in whom gastrointestinal surgery was planned and was permitted to drain throughout the surgical procedure. Oxygen was given intranasally when the anesthetic was given high in the spinal column and ephedrine was used intravenously at the beginning of the operation and intermittently when needed during the operation. Certain modifications of the Lemmon technique and apparatus are enumerated.

The continuous spinal anesthesia seemed superior because of three factors: (1) there is complete and sustained relaxation; (2) it does not necessitate hurrying on the part of the surgeon; (3) it is especially advantageous in patients with cancer because of the element of uncertainty in all exploratory procedures in which the operability must remain in question until the peritoneum is open. **MARY KARP M.D.**

Hingson, R. A.: Continuous Caudal Analgesia. *An Interim Report. J. Am. Med. Ass.*, 1944, 126: 1129.

The author reviews the status of continuous caudal analgesia on the basis of 42,000 parturients with comfortable labors and deliveries of babies born without narcotization and anesthesia. The average spontaneous breathing time of the baby from the moment the head was born was thirteen seconds, and the average lusty crying time was twenty-two seconds. The fetal mortality in this series was 1.7 per cent as compared with the fetal mortality of 5.2 per cent as registered for the entire United States. Sixteen maternal deaths occurred; 6 of these were attributed to obstetric complications, 7 to the misuse of caudal analgesia in unskilled hands and 3 were considered anesthetic deaths.

The author condemns the use of this method for the relief of discomforts of preliminary and early labor and advocates general anesthesia for the parturient in whom fear is uncontrolled.

The anatomy of the sacrum is reviewed. Malformations of the sacrum have been found to be more frequent than malformations of any other bone in the body.

The neurology of the cervix and uterus, from a study of 3,000 personally observed and managed obstetric cases, showed a natural anatomic dissociation between the motor and sensory components of the uterine nerves. Blocking of the eleventh and twelfth thoracic nerves was accompanied by total relief of abdominal cramps.

The three chlorides of Ringer's solution were considered the best diluent to intensify and prolong the

action of metycaine on the nerves in the peridural space

The hypotension which may occur is combated by the use of 50 mgm of ephedrine sulfate as needed, by the elevation of the extremities to be at right angles with the body and by the use of 100 per cent oxygen inhalations. The occurrence of this hypotension is utilized in the pre-eclamptic patient, in the eclamptic patient with convulsions, and in the medical case with essential hypertension. In all of these types of cases striking clinical improvement occurred immediately after the institution of the caudal analgesia. This improvement was probably due to the peripheral vasomotor dilatation of the pelvis and lower extremities and the vasomotor changes in the kidneys, with an associated increase in the output of urine. The method is suggested for the treatment of thrombophlebitis, sciatica, intractable pain of pelvic carcinoma, ureteral and vesical colic, Dietsch's burns of the lower extremity arterial emboli of the legs, and peripheral vascular angiospastic diseases. It is also indicated in operations below the umbilicus in the debilitated, aged, cachectic patient, and in the management of industrial and war trauma of the lower half of the body.

One hundred and sixty cesarean sections have been performed under this method without loss of mother or baby.

The malleable stainless steel caudal needle has almost eliminated the hazard of needle breakage. The urethral catheter has advantages for parturients who are unco-operative, and for those eclamptic patients who have lost motor control of their central nervous system. The continuous drip technique with modifications by Siever is mentioned. The latest modification is the author's introduction of the nontraumatic nylon needle which is inserted by means of a stiff steel stylet that is withdrawn as soon as the sacrococcygeal ligament is penetrated.

Emphasis is made on the newness of the continuous caudal analgesia technique, with a request for caution in its use.

MARY KARP M.D.

Hellman, L. M., Shettles, L. B., Manahan, C. P., and Eastman, N. J. Sodium Pentothal Anesthesia in Obstetrics. *Am. J. Obst.*, 1944, 48: 85

Between September 1, 1940 and March 31, 1944, 1,415 deliveries were carried out at the Johns Hopkins Hospital, Baltimore, under sodium-pentothal anesthesia.

The amount of sodium pentothal necessary for low forceps delivery together with episiotomy and repair lies between 0.75 and 1.0 gm. (from 15 to 20 cc. of a 5 per cent solution) provided that some form of sedation has been administered in labor such as a barbiturate or paraldehyde. For cesarean section 1.5 gm. (30 cc. of a 5 per cent solution) is the quantity usually required. The amount is never allowed to exceed 3 gm. Except in cases in which scopolamine has been given atropine (0.5 mgm. or 1/130 gr.) is routine. Due to mechanical difficulties this anesthesia is not suitable for spontaneous deliveries.

TABLE I.—ANALYSIS OF 963 OPERATIVE DELIVERIES UNDER SODIUM PENTOTHAL ANESTHESIA ACCORDING TO TYPE OF OPERATION

Low forceps	777	(80.7%)
Cesarean section	14	(1.5%)
Breech extraction	51	(5.3%)
Vernix and extraction	5	
Craniotomy	3	
Mildforceps	3	

Although the relaxation of the abdominal walls provided by sodium pentothal is not sufficient for many abdominal operations, it is quite adequate for cesarean section. Bleeding is less than with gas-oxygen-ether as is also in the authors' opinion, postoperative distention. Except for versions on second twins, sodium pentothal is ordinarily contraindicated for this operation because the uterus does not relax well.

There is a period of five minutes after starting the anesthesia during which the amount of drug reaching the fetus is very small and throughout the first ten minutes this amount is decidedly less, as a rule, than after fifteen or twenty minutes of the anesthesia.

TABLE II.—MG/100 BLOOD ACID PENTOTHAL IN MOTHER AND CHILD AT DELIVERY

Gm. of Sodium Pentothal given	Duration of Anesthesia in minutes	Mother MG/100	Infant MG/100
7	5	3.0	8
0.45	6	3.5	1.4
0.35	7	3.4	1.25
0.55	9	3.0	1.75
0.40		2.5	3.0
0.00	2	6.2	5.0
55	15	0.75	5

As far as the authors have been able to determine, there was no instance in the entire series of 1,415 cases delivered under sodium pentothal anesthesia in which the anesthetic agent was directly responsible for an infant's death or in which it played any demonstrable role.

It is the authors' impression that blood loss is less with sodium pentothal than with gas-oxygen-ether. The incidence of postpartum hemorrhage in the present series (600 cc. or more) was given as 2.8 per cent.

There were 2 maternal deaths in the series. Both patients were colored; they were nineteen and sixteen years of age, respectively; both were primiparas and both presented symptoms of severe toxemia of pregnancy.

Sodium pentothal has been employed successfully in approximately 500 additional obstetric operations not intended for immediate delivery of the infant—notably in puerperal tubal ligation, completion of incomplete abortion, artificial rupture of the membranes for the induction of labor and manual removal of the placenta.

EDWARD L. CORNELL, M.D.

Hayman, I. R.: *Experiences with Anesthesia in Combat Areas. War Med. Chic.* 1944 6 353

The duties of the anesthetist in the combat area includes not only the administration of the anesthetic agents but preoperative and postoperative care of casualties.

Shock therapy of the casualty patient is discussed with the related derangement of the cardiovascular and respiratory system. Respiratory emergencies are enumerated including the relaxed tongue foreign bodies, laryngospasm tension pneumothorax and open wounds of the chest. The immediate treatment of any condition that impaired tidal exchange included the administration of morphine tartrate in 1/4-gr doses however morphine was not given when head injury was possible or when increased intracranial pressure was evident. The use of oxygen or air under pressure, the intravenous injection of atropine, and intubation were the procedures of choice when laryngospasm occurred.

Tension pneumothorax is the result of a laceration of the the lungs and bronchi with the formation of a bronchopleural fistula. Treatment involves the reduction of the elevated intrapleural pressure and is most easily accomplished by the insertion of a short needle of wide bore.

It is important to recognize and treat the incipient insidious anoxia. A patient with slight anoxia may present a picture with symptoms of alcoholic intoxication, euphoria, ataxia, muscular weakness, impairment of muscular function, amnesia, and diminution of the special senses. The administration of oxygen by catheter or Boothby mask technique was used for this condition with gratifying results although the supply of oxygen which was available with the British in Tunisia was limited.

The available anesthetic drugs are outlined and the choice of an anesthetic agent is discussed. Pentothal sodium (given intravenously) was used far more than all other agents. It was usually necessary for the anesthetist to be responsible for several anesthetics going at the same time. For all abdominal operations anesthesia was induced with chloroform, ethyl chloride, or pentothal sodium followed by open or endotracheal ether-oxygen anesthesia. Most of the men with head injuries received treatment under local anesthesia. Spinal anesthesia was resorted to in only a few instances, as it was not considered suitable for battle casualties in the front lines within a few hours after injury one could not be certain of cardiovascular stability in spite of the apparent absence of shock. Block of the lumbar

sympathetic ganglions was performed in only a few cases in an attempt to increase the peripheral circulation of the lower extremities and blocks of the brachial plexus and of the median ulnar and radial nerves at the wrist were occasionally done for the surgical treatment of the arm and hand.

MARY KARP M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Shelden, C. H. and Pudenz, R. H. Improved Retractor for Hemilaminectomy *Surgery* 1944, 16 884.

In order to obtain adequate exposure for successful removal of protruded intervertebral discs Shelden and Pudenz constructed a retractor which facilitates hemilaminectomy. It consists of two blades of unequal lengths, the shorter having three long teeth which are inserted through the lumbar fascia adjacent to the spinous process. The longer blade is 2 inches wide slightly curved and has small laterally bent serrations on the free end these permit fixation at any desired depth in the muscle. The two blades are attached to the arms of a Liffenthal rib spreader which allows exchange of blades.

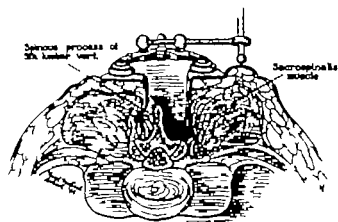


Fig. 1. Exposure for hemilaminectomy demonstrating method of muscle retraction.

The practical use of the retractor is shown in the accompanying illustration. Hemilaminectomy is simplified and exposure improved, particularly in patients having strong muscles. The instrument is adapted for use in the cervical region.

STEPHEN A. ZEEMAN M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Gomez, G. E.: The Present Value of Roentgenology in the Diagnosis of Appendicitis. *Am. J. Roentg.* 1944, 5: 624.

In this discussion on pathology of the appendix as determined roentgenologically the author bases his remarks on chronic and recurrent appendicitis and observations made on 21,000 gastrointestinal examinations and conclusions reached by other writers.

The author's conclusions relative to appendiceal disease are reached after careful examination of the gastrointestinal tract and gall bladder to eliminate these as the source of symptoms by careful and repeated examinations.

Having excluded the possibility of disease elsewhere he then searches for direct x-ray evidence of changes in the appendix, such as abnormalities in its size, shape, and position, and evidence of its physiological change such as its ability to fill and empty. The latter apparently has a direct bearing on its pathological state since an appendix which does not fill or delays in emptying itself is indicative of a disease process.

Indirect x-ray evidence of pathology is based on the reflex signs that can be elicited. These include pain over the appendix, pylorospasm which produces a six hour gastric retention and tenderness on palpation of the pyloric area, aerogastria in six hours, increase in size and density of the liver shadow and evidence of ileal spasm and ileocecal spasm.

On correlation of these findings with the clinical symptoms, the diagnosis of an active process can be determined.

R. A. BRASER, M.D.

Oppenheimer, A.: Roentgen Diagnosis of Incipient Cancer of the Rectum. *Am. J. Roentg.* 1944, 53: 637.

The author describes a technique for x-ray study of the rectum and sigmoid. In this procedure very small amounts of barium are employed and spot films or oblique films of the region in question can be made for the study of early lesions. While the method requires a little extra work the time consumed is not great and the results reward the extra effort.

A small rubber catheter is inserted into the rectum and with an attached syringe, controlled amounts of barium are gradually injected into the rectum to a desired filling. After roentgenoscopy and filming the catheter can be connected to the regular enema apparatus for further filling and study of the colon.

By this method the author has been able to discern small lesions of the rectum, particularly small malignant ulcers which would otherwise have been overlooked. Likewise, other intraluminal and extraluminal lesions, which would be obscured by the regular massive filling of the rectum, can be found and differentiated.

R. A. BRASER, M.D.

Vaughan, W. W., and Elchwald, M.: Priodax: A Contrast Medium for Cholecystography. Analysis of 163 Cases Outlining the Various Reactions in 3 Techniques and the Operative Findings in 22 Cases. *Radiology* 1944, 43: 578.

Cholecystography is a routine procedure in the study of gall-bladder disease. The high accuracy of this procedure (95 per cent) emphasizes the clinical importance of this study.

Since the original work of Graham and Cole on gall-bladder visualization by intravenous injection of tetrabromophenolphthalein, science has been striving constantly to improve the method by use of various chemicals and techniques. Tetraiodophenolphthalein was substituted for tetrabromophenolphthalein less than one year after the original (Graham Cole) publication and remained the chemical of choice until the recent advent of priodax.

The clinical use of priodax (bilmolecetan, as it was called in Germany) was first described by Kleiber in 1940. This dye was used on 55 patients and the results were verified by surgical exploration. In addition to the fact that it was an excellent contrast medium, it minimized the extent of diarrhea, nausea, and vomiting.

Priodax is a white, odorless powder soluble in alkali, ether, alcohol, and acetone, but almost insoluble in water. Experimental studies showed that the lethal dose with oral administration was 1,000 mgm. per kilogram of body weight. Fifty per cent of the priodax used is excreted through the urinary tract, in contrast to the 10 per cent of tetraiodophenolphthalein when the latter is used. The remainder of the tetraiodophenolphthalein is excreted through the gastrointestinal tract, which is undesirable from a roentgenographic viewpoint. Priodax is available in tablets of 0.5 gm. each, the dosage is 1 tablet per 25 pounds of body weight. Tablets should be swallowed with or without fluid, but should not be chewed.

The authors report a series of 163 cases in which priodax was used. The single-dose method was used in 51 cases; a divided dose was given in 55; and a double dose in 57 cases. The usual preliminary preparations were followed. In the single-dose method, 6 tablets were given following the fat-free evening meal; in the divided dose, 3 tablets were given following the noon meal and 3 following the evening meal; in the double dose, 6 tablets were given after the noon and evening meals.

Toxic effects with the use of priodax, given by the various methods, were infrequent and minimal in comparison with those following the use of tetraiodophenolphthalein. Roentgenologically the gall-bladder shadow was a little more dense with the use of the double-dose method; however it was satisfactory in all methods. For purposes of economy and standardization, the single-dose method is used.

In 22 of 226 examinations surgery confirmed the roentgen findings of a pathological gall bladder. In 1 instance of nonvisualization of the gall bladder a normal gall bladder was found at surgery. This patient, however, had clinical jaundice with an icteric index of 44.

MAURICE D. SACNA, M.D.

Heublein G. W.: The Roentgen Diagnosis of Traumatic Lesions of the Cervical Spine. *J Am Med Ass* 1944, 126: 950.

The author reports on the newer developments of apparatus and technique at the Percy Jones General Hospital Battle Creek, Michigan which permit an accurate roentgen diagnosis of traumatic lesions of the cervical spine and includes several valuable illustrations to prove his statements.

The acquisition of the Morgan meter which is not as yet in general use has helped considerably in the making of good roentgenograms of both simple and difficult projections of the cervical spine. The operation of the meter depends on the fact that intensity X exposure time = a constant. Thus if the intensity reaching the film is known in advance the time for proper exposure can be read off directly from a calibrated scale on the meter. By this method excellent roentgenograms can be obtained even through heavy plaster casts.

In addition to routine anteroposterior and lateral films at a distance of 6 feet, roentgenograms are being made through the open mouth in oblique (from 50 to 55 degree) projection and in the Jackson position, similar to an exaggerated Waters position which is used in the examination of the paranasal sinuses.

In this institution fractures of the cervical spine comprise 23 per cent of all spinal fractures. They are of two types: (1) those which affect the cord protecting portion of the spine, i.e. the neural arch and its processes and (2) those which affect the weight bearing structures of the spine i.e. the vertebral bodies. The latter vary from minute spicules projecting anteriorly or as a moderate bulge along the

anteroposterior border of the body to considerable compression of the spongy portion. Dislocations are observed with or without fracture, in sharp contrast to the dorsolumbar spine where dislocations almost invariably are associated with fractures. Soft tissue swellings adjacent to the vertebral bodies are also found to be of significance as they indicate hemorrhage, edema, or infection. In fractures of the arches callus formation often constitutes the most prominent feature.

Certain special procedures are also stressed by the author. Thus in not a few of the cases it is advisable to make roentgenograms in the lateral view with the neck in flexion and extension. Exposures made in flexion may show a subluxation not demonstrable in conventional views. In other instances delayed roentgenograms serve a better purpose. This applies especially to the fractures running through the base of the odontoid process which may be completely missing at the initial examination but may be revealed some weeks later after a rarefying osteitis has developed along the fracture line. Injuries to the intervertebral discs are often advantageously demonstrated by pantopaque myelograms. Successful delineation of such lesions however is not always an easy task.

Accurate diagnosis depends on several important factors such as (1) proper apparatus including canvas support and a special attachment for obtaining lateral films in the prone decubitus (2) adequate extension of the neck to prevent escape of the opaque material into the basal cisterns (3) experienced spinal puncture a factor which cannot be too strongly emphasized (4) proper withdrawal of the opaque medium at the end of the examination to be checked by a scout film of the area examined and (5) the closest correlation of the clinical and roentgenographic findings.

The general conclusion is reached that the roentgen examination is an invaluable aid in the diagnosis and differential diagnosis of traumatic lesions of the cervical spine.

T LYUCOMA, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Najjar, V. A., Holt, L. E. Jr., and Royston, H. M.: A Note on the Minimum Requirements of Man for Vitamin C and Certain Other Vitamins. *Bull. Johns Hopkins Hosp.* 1944, 75: 315.

A group of 7 young adults were given for a period of eighteen months a diet in which all water-soluble vitamins were provided as pure principles in carefully measured quantities. With the exception of thiamine, the intake of which was gradually reduced until deficiency symptoms appeared the vitamins were in quantities which did not vary throughout the entire experimental period. No symptoms of any deficiency other than that of thiamine were observed. These experiments do not define the minimal requirements of these factors, with the exception of thiamine, which is discussed elsewhere. They do however establish upper limits for the minimal requirement. Of particular interest are the observations on ascorbic acid, which confirm those of Pilgou and Losner that scurvy does not develop on a daily intake of from 8 to 25 mgm. of ascorbic acid.

Ruffin, J. M., Cayer, D. and Perlweig, W. A.: The Relationship between the Clinical Picture of a Mild or Early Vitamin Deficiency and Laboratory Determinations of Vitamin Levels. *Gastroenterology* 1944, 3: 340.

The frequency of full-blown vitamin deficiencies such as beri-beri, pellagra, and scurvy is decreasing rapidly and they no longer constitute a serious problem in North Carolina. It is reasonable to assume that for every advanced vitamin deficiency there must be many mild or early avitaminoses. It is difficult to determine whether one is dealing with a patient having a true vitamin deficiency or only a constitutionally inferior individual. Correct diagnosis is of greatest importance then for the intelligent use of vitamin therapy.

Recently laboratory procedures for measuring vitamin levels in the blood and urine have been devised and standardized. The application of these procedures in diagnosis may be extremely valuable if the patients with unquestionable evidence of vitamin deficiency prove to have significantly lower levels than normal controls. The authors undertook this study in an effort to determine if there was a relationship between early clinical vitamin deficiency and the laboratory determination of vitamin levels.

Two groups of patients were selected. The first, with vitamin deficiencies, were patients with glossitis, papillary atrophy of the tongue, cheilosis, or peripheral neuritis who showed the most reliable evidence of B-complex deficiency. All 26 patients selected gave a history of an inadequate diet and one or more of these findings. All were ambulatory free of or-

ganic disease, and without a history of recent vitamin therapy.

The second group were the controls who were again divided into a groups (a) patients with no definite evidence of a deficiency state and who ate the usual diet of an average tenant farmer. They presented a variety of neuroathenic complaints and represented constitutionally inadequate individuals with organic disease and (b) normal students, technicians, and dietitians, all of whom had been subsisting on an apparently adequate diet.

In evaluating the vitamin tests the figures comprising the lowest 10 per cent of the normal control group were arbitrarily selected as being the suggested lower limit of normal values since there was little agreement in the literature as to what constitutes the lower limit of normal.

The laboratory examinations for determining vitamin levels were carried out on blood plasma for vitamins A, C and carotene. B-complex vitamins were determined in the urine before and after a test dose, by chemical or biological assay.

The distribution of vitamin A and carotene levels showed a statistically significant difference between the normal controls and the deficiency group with the ward controls falling midway between the two. Although no clinical evidence of an A deficiency was observed in any patient, this study indicated that low levels of plasma vitamin A and carotene are likely to occur in patients in this locality with a mild deficiency of B complex.

The vitamin C values showed a wide discrepancy between the suggested lower limit of normal (0.15 mgm.) and the generally accepted value of 0.6 mgm. Nearly 50 per cent of the normal controls had values of vitamin C which fell below 0.6 mgm., and the authors believe this value is possibly too high. The higher vitamin C values are more apt to occur in normal individuals, but the distribution was so wide that there was no statistical significance between the two groups.

There were striking statistical differences between the two groups observed in the urinary excretion levels of nicotinic acid, riboflavin and thiamin, the greatest variations being found in nicotinic acid levels. There was little difference in the pyridoxine values of the two groups, which suggested that pyridoxine deficiency is not likely to occur in B-complex deficiencies, a point in keeping with the authors' clinical impression.

Most patients in the deficiency group had levels below the suggested lower limit of normal in more than one vitamin (22 of 26 when the B complex alone was considered, and 21 of 26 if vitamins A and C and carotene are included). Twenty-four of 26 patients classified clinically as having a B-complex deficiency had levels below the suggested lower limit of normal in nicotinic acid, riboflavin, or thiamin.

It appears then that patients having clinical evidence of a deficiency state based on the criteria enumerated are very likely to have levels which fall below the suggested lower limit of normal in one or more members of the B complex. If observations made in this study are confirmed by subsequent study laboratory determinations may become useful procedures in the recognition of early deficiency states.

ROBERT BUCKLOW M.D.

Volpitta P. P., Woodbury R. A., and Abreu B. E.: The Influence of Different Forms of Mechanical Artificial Respiration on the Pulmonary and Systemic Blood Pressure. *J Am Med Ass* 1944 126 1066.

An improved technique has been developed for the measuring of the effective pulmonary and the effective systemic blood pressure in animals with a closed chest. The pulmonary and systemic blood pressures have been recorded while respiration was maintained with the individual use of seven resuscitators.

One sound was inserted into the exposed left carotid artery on into the aorta, past the semilunar valves, and into the left ventricle. The other sound was inserted into the exposed external jugular vein down to the superior vena cava and right auricle into the right ventricle.

Cardiac arrest was produced (1) by complete occlusion of the airways in 3 dogs (2) by use of the bellum with carbon-dioxide-absorption technique in 3 dogs and (3) by electrically induced ventricular fibrillation in 3 dogs.

No matter what method of mechanical artificial respiration was used, recovery of the animal was accomplished when respiratory arrest and slow, weak cardiac contractions were produced by the administration of helium with the carbon-dioxide-absorption technique. No significant change was produced in the pulmonary and systemic blood pressures with any of the methods of resuscitation studied.

Any blood flow produced by the resuscitators did not reach the coronary and cerebral arteries. On the other hand blood was pushed toward the extremities and cutaneous areas.

Intrapulmonic positive pressure greater than 10 or 12 mm. of mercury if maintained for a prolonged period of time may hinder venous return to the right side of the heart.

RICHARD J. BENNETT JR. M.D.

Henry, F. M., Lawrence, J. H., Bridge, E. V. and Williams, O. L.: Protective Effects of Preoxygenation on Abdominal Gas Pain; Results of a Study of Preflight Breathing of Oxygen on Pain Resulting From Decompression to 23,000 Feet. *War Med., Chic.*, 1944, 6 395

The denitrogenation resulting from the breathing of oxygen has been reported to relieve postoperative and obstructive abdominal gas distention in human beings and has been found to reduce the total amount of gas in an isolated intestinal loop in dogs.

Radioactively labeled inert gas introduced into the stomach and lower part of the bowel of human subjects is excreted by the lungs in proportion to the pressure gradient. Swallowed oxygen would be expected to cause less trouble than swallowed air because of its additional metabolic elimination. In view of these observations it occurred to the authors that the incidence and severity of pain due to the expansion of gas in the digestive tract resulting from decompression in an altitude chamber or in an aircraft might be reduced by the preflight breathing of oxygen.

A control series of 80 healthy young males was decompressed twice to 38,000 feet and exercised at that altitude for ninety minutes. Breathing of pure oxygen began nine minutes before the altitude was reached. A similar group made three ascents under the same conditions except that the breathing of oxygen began one third hour one hour and two hours before the altitude was reached. 61 of these subjects made all three ascents.

In 20 per cent of the controls definite gas pain developed with prebreathing of oxygen for one third hour the incidence dropped to 23 per cent with one hour it was 10 per cent and with two hours only 10 per cent. Moderately severe gas pain occurred in 8.4 per cent of the subjects in the control runs, in 5.8 per cent in the one third hour runs and in 2.7 per cent in the one hour preoxygenation runs. No pain of this or greater severity occurred with two hours of preoxygenation.

Detailed examination of the data yields no evidence that differences in decompression experience diet or elapsed time between meals and ascent can account for the observed protection.

Definite gas pain appears to have a higher incidence if decompression occurs three hours after eating than is the case if the elapsed time is only one or two hours.

It is concluded that two hours of preoxygenation causes a decided reduction in the incidence and severity of abdominal gas pain resulting from decompression to 38,000 feet (11,400 meters).

JOHN E. KIRKPATRICK, M.D.

Kritzer, R. A.: Acute High Altitude Anoxia; Gross and Histological Observations in 27 Cases. *War Med., Chic.*, 1944, 6 369.

Fatalities in air crews, due to deprivation of oxygen during bombing operations at high altitude, have afforded an opportunity to study the gross and microscopic anatomy of acute anoxia in man as it occurs at a low atmospheric pressure.

In 1942 Mueller and Rotter described 4 cases of acute high-altitude anoxia among air crews of the Luftwaffe. They found congestion of all organs of the greater circulation which they attributed to right ventricular failure and to peripheral vascular collapse. In all cases these authors noted an absence of clotting of the blood. Fat free vacuoles, either optically empty or partially filled with refractive granules staining lightly with eosin, were present in

the livers of all patients. In heart muscle cells the vacuoles were observed to be adjacent to and deforming the nuclei, and they were frequently arranged in continuous strands appearing as a "string of pearls." The vacuoles were considered similar to those described by Pichotke, Hesse-Ladewig, and Trowell.

Twenty-seven autopsies were performed during 1943 in one hospital on members of high-altitude bomber crews in whom death had been attributed to anoxia by the Air Force medical officers who investigated the cases. In no instance was the analysis of the history complicated by the presence of wounds. In no case was a rapid ascent to high altitude recorded. Although the possibility of fatal air embolism was not considered likely at the altitude at which death occurred a search for intravascular gas in the right ventricle and in the mesenteric veins was made in 16 successive cases. None was found. In general the casualties occurred at altitudes of from 24,000 to 31,500 feet (7,300 to 9,630 meters), but in many instances the precise level at which difficulty was encountered could not be determined because the exact time of death was not always known by crew mates.

A study was made of the findings at autopsy in 27 cases of acute high-altitude anoxia. Widespread, severe capillary congestion was found. This was conspicuous and most constant in the pulmonary renal, intestinal, and cerebral capillaries. The skeletal muscle did not have this congestion. In a high proportion of cases the systemic venous and the portal circulations showed gross and microscopic congestion, and the right ventricle was dilated. There was wide individual variation in the incidence, location, and amount of edema and hemorrhage. An exception to this was the consistent occurrence of hemorrhage in the thymus and in the middle ear. Swelling of the endothelial cells of capillaries of the renal medulla was observed. The presence of fat-free and glucogen free vacuoles, previously described, in the myocardium and liver and less frequently in cells of other organs, was confirmed. These vacuoles occurred with equal frequency in cases of anemic anoxia (acute carbon monoxide poisoning) but were rarely found in the tissues in nonanoxic control cases.

JOHN E. KIRKPATRICK, M.D.

Brues, A. M., and Shear, M. J.: Chemical Treatment of Tumors. Reactions of 4 Patients with Advanced Malignant Tumors to Injection of a Polysaccharide from *Serratia Marcescens* Culture Filtrate. *J. Nat. Cancer Inst.* 1944, 5, 95.

Certain preparations of bacterial origin when administered parenterally to animals bearing sarcomas produce hemorrhage in the tumors within a few hours. The action is highly selective, for while severe hemorrhage is induced in the tumor it has not been reported to occur in any of the normal tissues with a few minor exceptions of slight degree. The hemorrhage and necrosis produced in this way are followed in some instances, by complete and permanent regression of the tumor.

The bibliography on the treatment of human tumors with induced bacterial infections or with bacterial products began about seventy five years ago. Interest in the effect of bacterial preparations on tumors in experimental animals was revived in 1931 by the report of Gratia and Linx. Because of the high toxicity of such bacterial preparations, Shear and Andervont separated the active agent from toxic and inactive constituents. They obtained a polysaccharide fraction from filtrates of cultures of *Serratia marcescens* (bacillus prodigiosus) one of the organisms used in the preparation of "Coley's mixed toxins."

This product was used by the authors in 4 patients with advanced malignant tumors (prostatic carcinoma, lymphosarcoma, multiple myeloma, and Ewing's sarcoma) in the form of muscular injections. All of the patients died with tumors. Two patients showed noteworthy relief of their symptoms. To showed evidence of hemorrhage in the tumors at postmortem examination, although it was not possible to decide whether this finding was related to the treatment. The patient with multiple myeloma showed no evidence of any effect of this agent on the tumor.

Following initial chill and fever, a prolonged period of hypotension, sometimes with anuria and cardiac decompensation occurred. Some of these reactions may have been the consequence of rapid absorption of products of destruction of the tumor tissue.

The 2 patients showing symptomatic relief also showed chemical evidence of the rapid breakdown of nitrogenous substances. This fact suggested that tissue protein including nucleoprotein might have been destroyed.

The findings in this preliminary study do not warrant the conclusion that this polysaccharide should be recommended in the treatment of patients with malignant tumors. The reactions in 2 cases, taken in conjunction with the results of animal experimentation, suggest that further investigations may yield interesting results. However great caution must be exercised even in the experimental employment of this material in patients. Small doses may provoke violent reactions, and death may follow in a short time unless precautions are taken to counteract the undesired responses.

JOSEPH K. NARAT, M.D.

GENERAL BACTERIAL, PROTOZOAN AND PARASITIC INFECTIONS

Hodges, R. G.: The Use of Sulfadiazine as a Prophylactic against Respiratory Disease. *J. Experimental Med.* 1944, 31, 817.

In this experimental problem in which sulfadiazine was used as a prophylactic measure against respiratory diseases, the author had somewhat of an ideal condition for experimentation. The two groups of individuals used for controls and studies had been observed over a period of time before the experiment, and lived under similar environmental circumstances.

Since these groups were under close supervision the date obtained is worth consideration.

The effect on total respiratory disease after the administration of 2 gm of sulfadiazine per day reduced the incidence to one-third and one-half of the control group. Throughout the experiment a variety of dosages were tried. No definite amount is recommended but an optimal amount for a given group should be worked out individually. No serious untoward reaction occurred in this study.

The most striking effect was obtained in streptococcal sore throat and scarlet fever in which the incidence dropped to zero.

In pneumococcal infections there was a significant drop, but since there was also a decline in upper respiratory infections the drop was hard to evaluate. Atypical pneumonia, likewise, displayed a low incidence but the number of cases were too few for significant analysis.

Acute rheumatic fever was less prevalent during this study and fell below the expected rate.

R. A. BRIDGER, M.D.

DUCTLESS GLANDS

Broders, A. C., and Parkhill, E. M.: Diffuse and Adenomatous Goiter and Goiter Induced by Various Agents. *Surgery* 1944 16 633

The diffuse colloid goiter which used to be observed frequently from prepuberty to late adolescence according to Haines is rarely observed today by the clinician. Furthermore it is almost never seen by the surgical pathologist.

Since the advent of administration of a compound solution of iodine the typical meaty exophthalmic goiter is seen much less frequently and has for the most part been replaced by a gland comparable to a colloid goiter although smaller. The change in the exophthalmic goiter also is undoubtedly attributable to administration of the compound solution of iodine. Following the administration of a compound solution of iodine, the epithelium changes from columnar to a low cuboid or flat type and the acini dilate or at least have larger lumina, and their colloid content is increased. This increase in the size of the lumina is probably the result of the diminution in the size of the cells. Some exophthalmic goiters on the other hand, are more or less resistant to the changes that usually take place after the administration of a compound solution of iodine.

The nodules sometimes observed in hypertrophic parenchymatous thyroid or exophthalmic goiters with or without adenomas differ from the true adenomas of exophthalmic goiter in that they are not encapsulated rarely contain true fetal acini, and under the microscope usually resemble the extranodular part of the goiter. In other words the nodules are to a large extent comparable to the nodules observed in hyperplasia of the prostate gland.

In all hypertrophic parenchymatous thyroids or exophthalmic goiters that is in the diffuse non-nodular the nodular and the adenomatous types,

varying degrees of chronic thyroiditis may be present. The chronic thyroiditis in these goiters is characterized by fibrosis and lymphocytic infiltration of the interfollicular tissue with or without the formation of germ centers. This inflammatory reaction is probably attributable not to bacterial activity but to toxic products of the goiter. To some extent this form of thyroiditis may be activated by a compound solution of iodine as it has been more in evidence since the therapeutic use of such a solution of iodine began.

Adenomas may occur singly but usually they are multiple. They vary markedly in size in consistency and from a light amber to a reddish brown in color and they are encapsulated. They may undergo various types of degeneration, such as hemorrhagic, fibrous, hyaline calcareous lipoid (granular) and cystic. Macroscopically and microscopically true adenomas differ from the surrounding thyroid tissue.

In recent years certain interesting and important forms of goiter have been observed after the administration of a variety of agents. Some of these goiters are now coming to the attention of the pathologist.

One of the first of these forms of goiter to be noted in man was that seen in patients receiving thiocyanates over a prolonged period in the treatment of hypertension.

Goiter produced by thiocyanates in many respects resembles a form of experimental goiter of great interest since it was first reported by Chesney, Clawson and Webster in 1928, the so-called 'cabbage goiter' or 'cyanide goiter'.

The cabbage goiters and the cyanide goiters like those produced by thiocyanate can be prevented by the simultaneous administration of iodine. The administration of iodine after the development of goiter in rabbits however resulted in the onset of symptoms of severe sometimes fatal, hyperthyroidism.

Other important compounds recently found to have powerful goiter-producing effects fall mainly in two groups (1) thiourea and various thiourea derivatives, and (2) sulfonamides and related substances.

Kennedy in 1942 reasoning that the goiter producing effect of rapeseed might be due to a derivative of urea, injected allylthiourea into rats and found that it produced large goiters. Richter and Clisby in 1942 produced marked hyperplasia of the thyroid of rats by the administration of phenyl thiocarbamide. MacKenzie, MacKenzie and McCollum in 1941 found that the administration of sulfaguandine to rats resulted in enlargement of the thyroid and in 1942 MacKenzie and MacKenzie produced goiters by administering thiourea, diethylthiourea, and allylthiourea as well as sulfaguandine and other sulfonamide compounds. Astwood, Sullivan, Bissell, and Tykowitz in 1943 produced enlarged thyroid glands in rats with both sulfonamide compounds and thiourea.

It is of interest that the experimental production of goiter by cyanides and thiocyanates has been prevented by the simultaneous administration of iodine whereas the goitrogenic effect of thiourea, sulfanilamide and related compounds cannot be prevented

by the administration of iodine but can be prevented by the administration of desiccated thyroid or thyroxin. The administration of desiccated thyroid or thyroxin was also effective in reducing goiters after they had developed regardless of whether they had followed the administration of cyanides, thiocyanates, thiourea, or sulfonamide compounds.

It has been assumed that the action of the various drugs which produce goiter is by means of an inhibition of, or interference with the manufacture of the normal thyroid hormone. The resulting increase in activity of the thyroid-stimulating pituitary hormone brings about hyperplasia of the thyroid cells but does not bring about an increase in thyroid hormone which is in fact reduced to subnormal levels. This inhibitory effect has been made use of clinically by the administration of thiourea or thiouracil to patients suffering from hyperthyroidism in the form of Graves disease. In addition to the disappearance of toxic symptoms and a decrease in the basal metabolic rate temporary increase in the size of the thyroid gland was observed in 3 of 9 patients treated with thiouracil by Williams and Bassell. Microscopically the thyroid gland in cases of Graves disease treated with thiouracil shows extreme hyperplasia with heightened epithelium, marked papillary infolding, and mitosis in the epithelial cells.

The authors said that in the thiocyanate goiter there is more cellular hypertrophy and it is therefore, more nearly comparable microscopically to an exophthalmic goiter and that the thiouracil goiter is

more of a cellular hyperplasia with mitosis very much in evidence and is therefore more comparable to a carcinoma of the thyroid.

Mahorney II: Goiter in the Southern States. *Surgery* 1944, 6 764.

Goiter is more common in the southern states, than it had been generally believed. It is more common in southern Louisiana than in the northern part and more common along certain bayous.

The surgical mortality is higher in the South and the surgical mortality of goiter is definitely higher in the negro than in the white man. The author thinks that this is due not so much to the greater severity of the disease in the negro but to the poorer physical surroundings before and after operation and hence the less prompt preoperative and postoperative response.

The author's material consisted of 101 patients who underwent 110 operations of these 7 were multiple-stage operations. Sixty-one patients were white and 40 were negroes. Fifty-five patients presented toxic goiters. There were 2 postoperative deaths, both of which might have been prevented by multiple-stage operations.

The author thinks that the negro should be added as a third group to the groups of the elderly and of the young who do not tolerate surgery well. Added cautiousness is necessary to determine the proper time and extent of the operation in the negro.

FRED S. MOORE, M.D.

June, 1945

International Abstract of Surgery

*Supplementary to
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INTERNATIONAL ABSTRACT OF SURGERY

VOLUME 80

JUNE, 1945

NUMBER 6

GAS GANGRENE

Collective Review

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GAS gangrene is a companion of wars and is worthy of serious reconsideration now that we are once again engaged in a world wide conflict. MacLennan (26) reports that in Africa and the Middle East, from September 1939 to October 1942 1 in 300 of the wounded had gas gangrene and half of those so infected died. Monroe (33) states that in the Southwest Pacific 1 in 150 developed gas gangrene, and if débridement was done within from four to six hours, there was a 40 per cent mortality but after another battle when no débridement was done and sulfonamide was given within from four to six hours (inadequate dosage) the incidence of gas gangrene was six times as high. In World War I reports are similar. In civilian accident cases, the incidence is lower and the mortality similar (30-46). Cramp (10) gives the incidence at Bellevue Hospital New York in 1912 as 1 in 600.

Unfortunately the literature discloses marked disagreement regarding the best method of treatment. Surely a disease of such high incidence and high mortality should be re-evaluated diagnostically and therapeutically.

DIAGNOSIS

Although more attention has been given to the diagnosis of gas gangrene in the present war the incidence has not changed appreciably during the last twenty five years, as evidenced by the incidence of 0.36 per cent in 1917 and 1918 and the present incidence of 0.32 per cent (28). The American Expeditionary Forces reported an incidence of 1.7 per cent in 1917 and 1918.

Gas gangrene was recognized as a clinical entity during the days of Hippocrates. However it was not until 1607 that one of the first clinical

descriptions was reported by Fabricius Hildanus (37). Subsequently the attention of the medical profession was directed to this disease during the Crimean War and American Civil War. As wars continued greater stress was placed upon the importance of early diagnosis and treatment of gas gangrene. Intensive studies were made during World War I and are being continued during the present conflict.

Gas gangrene presents a composite clinical picture (19) and should be differentiated from "an aerobic cellulitis" and "gas abscess," inasmuch as the presence of gas-producing organisms in a wound is not sufficient evidence to warrant the diagnosis of gas gangrene.

Anaerobic cellulitis may start as a simple contaminated puncture wound with no muscle involvement. The onset is gradual, and usually three or four days are required for the cellulitis to develop fully. Salient clinical findings of anaerobic cellulitis are: abundance of gas, foul odor, practically no skin changes or swelling, no pain and very little toxicity. On the other hand gas gangrene may be evident within a few hours of a given injury; the patient becomes extremely toxic; he suffers from severe pain, marked swelling and discoloration of the skin; appear a characteristic sweetish odor permeates the patient's surroundings and a moderate amount of gas is present in the tissues. (Gas in tissue may be visualized first in the roentgenogram.) Fortunately gas gangrene is much less frequent than the benign anaerobic cellulitis. Nevertheless, there is always the potential danger that some of these cases will develop gas gangrene.

Nightingale (35) divides this disease into four groups: (1) acute fulminating gas gangrene, (2) gas gangrene of the muscle, (3) gas abscess and

(4) subcutaneous gas infection. In his opinion, only the first two groups should be called "gas gangrene." The latter two should be classified as wounds with gas infection and should not be included in the statistics of gas gangrene. Sewell *et al.* (42) advocate the following diagnostic criteria: (1) positive clostridium-welchii culture (or vibrio septique) (2) spreading infection (3) gas in the tissues, and (4) discoloration and edema of the involved structures. They suggest the term gas cellulitis or clostridium cellulitis to include mild or borderline cases.

ETIOLOGY

The micro-organism *clostridium welchii* (47) was reported in 1893 and 1900. Shortly thereafter the vibrios septique and bacillus oedematiens were described as contributing causative organisms.

As the study of gas gangrene progressed, many more organisms were isolated. At present there are about 20 species (37) belonging to the clostridia group. For practical clinical purposes, the chief micro-organisms causing gas gangrene in order of prevalence are the *clostridium welchii*, *oedematiens*, *septicum*, and *histolyticum*. The pathogenicity is due to the toxins given off by the clostridia. These virulent organisms may be found alone or in combination, and when multiple organisms are present the fatality rate is increased. The worst is the *clostridium histolyticum*, for which no effective antitoxin has yet been developed. Its proteolytic action on living and dead tissue is maximal. MacLennan (27) reports it to be 100 per cent fatal. It is never found in the benign "anaerobic cellulitis."

Anaerobic bacteria may be found as normal inhabitants of the intestinal tract of man and animals. Their spores are also very plentiful in cultivated and fecally contaminated soil. These bacteria have a low pathogenicity for man and exist as saprophytes. However if they are introduced into a wound containing devitalized tissue, they multiply rapidly and may prove fatal. Devitalized muscle is an excellent culture medium for clostridia.

The source of the bacteria causing gas gangrene is still an unsolved problem. Some authors (2) are of the opinion that the bacteria are prevalent in wet, cold weather and in manured soil. Such soil was found to be present in Flanders from 1914 to 1918 and from 1939 to 1940. Other authors do not believe the soil content to be an etiological factor. Wall (44) states there is no soil more contaminated than that of the Yangtze delta in the region of Shanghai however there

have been very few cases of gas gangrene in this area. The African and Middle Eastern deserts (27) showed practically no clostridia when troops were in movement, but as soon as these troops camped for any length of time the clostridia were plentiful.

It is believed that woolen clothes (2, 18, 30) may be an etiological factor inasmuch as sheep are a major source of anaerobic bacteria and in cold climates, where woolen clothing is required, the incidence of gas gangrene is usually increased. To prove this theory Macs examined wool, cotton, and silk clothing: some samples were dry-cleaned and steam-pressed the remaining samples were untreated. Gas-forming organisms were found in almost all of the woolen samples, whether cleaned or not. No organisms were found in cotton or silk. Anaerobic bacteria have been found in the clothing of soldiers in the Middle Eastern theaters of the present war. The incidence of gas gangrene in the Italo-Ethiopian War and the Middle Eastern and African campaigns, in which the soldiers wore cotton clothing, has been low compared to that on the European continent where woolen clothing was worn. In any given battle, the incidence of gas gangrene may be increased or decreased according to the type of wound sustained. Bullet wounds would not show as high an incidence of gas gangrene as would wounds from high explosives, shells, or bomb fragments.

TREATMENT

As mentioned heretofore, there has been little change in the incidence or mortality of gas gangrene during the last twenty-five years. Treatment may be surgical, serological, chemical, radiological, or any combination of the four. Unfortunately not many advocates of a given method are in accord as to the efficacy of that method or any combination of methods. Consequently practically the entire medical armamentarium has been tried, and it would seem almost impossible to credit any one method with cure.

Theoretically gas gangrene should be prevented by adequate surgery, but such is not always the case. Results (28) in the Middle Eastern theaters of war are not too satisfactory. Of 124 cases of gas gangrene, 64 had had prophylactic surgery. Of 17 cases of anaerobic cellulitis, 7 were treated surgically. It is possible that debridement as done in the battles of the Middle East was not as radical as that done in 1917 and 1918.

Adequate debridement (48, 49, 50) should be done as soon as possible in an effort to avoid the onset of gas gangrene. The limb should be im-

mobilized and the body kept warm but heat should not be applied to the affected area. Embarrassment of the circulatory system should be avoided. Tight dressings, packings, or casts should not be used. A sympathetic block is preferred whenever vasospasm is present. Hematomas should be excised to relieve tension. If possible, foreign bodies are removed. The incidence of contamination increases if the wound is deep and irregular. Wounds of this type should be left open with adequate drainage (37). Diseased muscle should be excised. Alfonso (1) recommends its removal by cautery or surgical diathermy, however there is no other evidence in the literature that removal by cautery is effective. Gas gangrene per se is not sufficient to warrant an amputation. On the basis of his experiences in North Africa MacLennan (29) states "It is, unfortunately still the constant endeavor of certain surgeons in the Middle East and elsewhere to amputate or attempt to amputate each and every case of gas gangrene of the extremities. Amputation should be done when the condition of the limb would require amputation, even were no gas present."

The mortality of gas gangrene was reported by the A.E.F. in France to be 48.15 per cent. Millar reported a mortality of 49.7 per cent in 567 cases collected from civilian life. Coleman and Bennett (8) collected 41 cases of which 7 were treated by amputation with no deaths. 6 had amputation plus serum with 1 death. Swan (43) reported 9 cases of gas gangrene in the battle of Dunkirk. Amputation was done in 4 and an incision followed by the use of hydrogen peroxide serum, and sulfanilamide was made in 5. All 9 patients recovered. Fifteen cases of anaerobic cellulitis were treated with serum and sulfanilamide and the results were good.

The value of gas-gangrene serum still remains undetermined. Statistical clinical evidence is meager (5, 38, 50). In many cases in which it was used the dosage was either under or above the recommended one. Qvist (36) states that the mortality was 18 per cent when serum was used and 50 per cent when it was not used. Ghormley (13) reports a mortality of 13.4 per cent when serum was used and 44.5 per cent when it was not used. MacLennan reports that of 8 patients treated with serum, 2 (25 per cent) died and of 58 treated with serum and sulfonamides, 19 (33 per cent) died. The National Medical Research Council advocates the use of serum. However Kelly and Dowell (22) state that in their experience patients with diabetic gas gangrene do better without serum.

Sulfonamide therapy is used locally orally or both ways. Experimental and clinical evidence (40, 42) is not very encouraging. Of all the sulfonamide derivatives used sulfathiazole and sulfadiazine have shown the best results. Using neoprontol sulfanilamide, and sulfapyridine Hendricks (23) reports a mortality of 89.5 per cent in guinea pigs. Hawking (17) found that the local use of sulfanilamide sulfapyridine sulfaguanidine and sulfadiazine was not effective whereas the results with sulfathiazole were fair. Sandusky and Meleney (39) and Hac (14, 16) believe that the results in animals would be better if the drug were given within two or three hours of the development of gas gangrene. It was not effective when gas gangrene was permitted to become well established.

The use of sulfonamide drugs has not influenced the incidence of gas gangrene. The Bulletin of the United States Army Medical Department states that the prophylactic local and general use of sulfonamides has not prevented wound infection. The National Medical Research Council (Meleney, 32) reports that the use of sulfonamides prevents systemic invasional infection and thereby lowers the mortality rate. MacLennan states that of 43 patients who were given adequate doses of the sulfonamide drug, 22 developed gas gangrene. In his series of 28 cases treated with sulfonamides the mortality was 19 per cent. However he is optimistic with regard to the use of serum and sulfathiazole combined. In a second report of 44 cases of gas gangrene with a 30 per cent mortality MacLennan attributes the results to good surgery and intensive chemotherapy. Lyons (25) believes that there is a distinct trend away from local sulfonamide therapy. Sulfasuxidine therapy in wounds of the buttocks is indicated in order to eliminate organism contamination of the intestines.

The successful use of irradiation in gas gangrene was first described by Kelly and Dowell in 1928 (21). However experimental evidence (in animals) for the continued use of irradiation has been poor. Weed *et al* (45), Erb and Hodes (12) and Caldwell and Cox (7) all report poor results in guinea pigs, mice, pigeons, and in experiments *in vitro*. Bisgard *et al* (3) using rabbits, report that irradiation provided protection against a lethal culture in from twenty-four to forty-eight hours. These authors believe that x rays produce an antitoxic substance which neutralizes the effect of bacterial toxins.

Contrary to experimental evidence clinical reports (9, 11, 21, 22, 41) have been favorable. Kelly and others believe there is a distinct differ

TABLE I—TYPES OF INJURY OR DISEASE

	Prophylactic irradiation of compound fractures, etc.	Gas cellulitis	Gas gangrene
Total No. of cases	8	8	55
Trauma	7 ¹	5	31
Gunshot or stab wounds	3	—	6
Diabetes or arteriosclerosis	7	3	4
Post surgical	—	—	4

ence between the results obtained in the treatment of animals and those obtained in the treatment of human beings. Anderson and Olin studied 71 cases, of which 63 did not receive irradiation and 43 terminated fatally a mortality rate of 68 per cent. Two of the 8 patients treated by irradiation died a mortality of 25 per cent. Coleman and Bennett (8) reported a mortality of 71 per cent with irradiation, death occurring in 10 of 14 patients.

It is well to remember that although the total number of cases reported by each author is comparatively small, Kelly and Dowell reported a mortality rate of less than 10 per cent for a group of 200 cases collected from all sources. They are of the opinion that irradiation is a must in the treatment of gas gangrene. Some surgeons question this remarkably low mortality rate and believe some of these cured cases to have been anaerobic cellulitis. However other surgeons have seen such dramatic results with the use of irradiation that they recommend prophylactic irradiation for all compound fractures. Bowen (4) reports on 40 cases treated prophylactically 2 of the patients developed gas gangrene but none died. Bowen states that his surgical colleagues believe that the average lesion heals faster and that there is less mixed infection with preliminary irradiation. Mowat (2) reports that with prophylactic irradiation there is a marked and rapid reduction in traumatic edema, and relief from pain within the first twenty four hours none of his cases developed gas gangrene. Keating and Davis (20) recommend the use of prophylactic irradiation.

SAN FRANCISCO COUNTY HOSPITAL SURVEY

A series of 145 cases which was observed over a ten-year period from 1934 to 1944 at San Francisco County Hospital was reviewed by the author. Gas gangrene was present in 55 cases and gas cellulitis in 8, while prophylactic irradiation against gas gangrene was given in 82 cases. The gas-gangrene series was divided into two groups, those seen from 1934 to 1937 and those seen from 1937 to 1944. In the first group surgery was the

TABLE II.—PROPHYLAXIS

(Cases observed in San Francisco City and County Hospital Survey)

Type of treatment	Prophylactic irradiation against gas gangrene (817-83)	Gas cellulitis (834-84)	Gas gangrene (835-84)
Surgery	—	3	15
Surgery and serum	—	—	10
Surgery and radiation therapy	3	—	—
Surgery and sulfonamides	—	—	4
Surgery serum and sulfonamides	—	1	5
Surgery serum, sulfonamides, and radiation therapy	15	—	1
Surgery serum and radiation therapy	5	—	—
Surgery sulfonamides and radiation therapy	—	—	—
Serum	—	—	2
Sulfonamides	—	—	3
No treatment	—	—	2
Total Cases	82	8	55

dominant therapeutic measure, but beginning with 1937 radiation therapy and sulfonamide drugs were added. During the latter period, some of the surgeons were so impressed with the results of irradiation that they requested that all compound fractures be given prophylactic irradiation. Consequently from 1937 to 1943 another group was treated with surgery and irradiation as the prime therapeutic measures.

In the majority of the 145 cases, the primary cause of the disease was trauma. There were several patients with diabetes, arteriosclerosis, and post surgical gas gangrene. (The initial injuries or diseases are listed in Table I.)

Prophylaxis was as follows:

Prophylactic surgery was done in combination with radiation therapy on 32 of the 82 patients having compound fractures, etc. surgery was done in combination with serum, sulfonamides, and radiation therapy on 25 surgery was done in combination with serum and radiation therapy on 15 and surgery was done in combination with sulfonamides and radiation therapy on 10. Two patients developed gas gangrene but the irradiation was continued and they recovered.

Prophylactic surgery alone was performed on 3 of the 8 patients with gas cellulitis, surgery was performed in combination with sulfonamides on 2 surgery was performed in combination with serum and sulfonamides on 1 and surgery was performed in combination with serum, sulfonamides, and irradiation on 2.

Prophylactic surgery alone was done on 15 of the 55 patients with gas gangrene surgery was

done in combination with serum on 10 surgery was done in combination with radiation therapy on 1 surgery was done in combination with sulfonamides on 4 surgery was done in combination with serum and sulfonamides on 5 surgery was done in combination with serum sulfonamides and radiation therapy on 2 surgery was done in combination with serum and radiation therapy on 1 serum alone was given to 2 sulfonamides alone were given to 3 and no prophylactic treatment was given to 12 (The prophylactic treatment in all three series is listed in Table II.)

With regard to the thirteen patients with gas gangrene who were seen in the period from 1934 to 1937 (including the 3 patients who entered the hospital in extremis) surgery alone was performed on 6 surgery was performed in combination with serum on 5 surgery was performed in combination with radiation therapy on 1 and serum alone was given to 1.

With regard to the 42 patients with gas gangrene who were seen in the period from 1937 to 1944 (including the 4 patients who entered the hospital in extremis) surgery and irradiation were the chief therapeutic measures. Surgery was done in combination with serum on 3 patients surgery was done in combination with roentgen irradiation on 5 surgery was done in combination with serum and sulfonamides on 4 surgery was done in combination with serum sulfonamides and roentgen irradiation on 10 surgery was done in combination with serum and roentgen irradiation on 6 and surgery was done in combination with sulfonamides and roentgen irradiation on 5 (Details of therapy and results are listed in Tables III, A and B.)

Thirty two of the 42 patients (1937 to 1944) were given serum as part of the treatment (a therapeutic dose of serum was given to 28) 17 (53 per cent) recovered of the 15 who died, 13 had been given a therapeutic dose. Sulfonamides were used in 28 instances and were given locally to 5 patients 14 (50 per cent) recovered. Although the drug was given early and in amounts that were adequate the derivatives were changed from day to day. Of the 35 patients who were given roentgen irradiation, 23 (66 per cent) recovered. The irradiation was given to the amputation stump of 17 12 of these recovered. Irradiation therapy was given to the involved area of the other 18 patients and 11 of these recovered. In 3 fatal cases, irradiation had been given as a last resort when the patients were in extremis. It is noteworthy that in 5 cases with recovery, irradiation was the only therapeutic agent used in combination with surgery. In addition to sur-

TABLE III A—TREATMENT AND RESULTS

(Thirteen cases of gas gangrene seen at San Francisco City and County Hospital, 1934 to 1937)

Type of treatment	Recovered	Died	Died (Entered hospital in extremis)	Total
Surgery	1	2	3	6
Surgery and serum	2	3	—	5
Surgery and radiation therapy	1	—	—	1
Serum	—	1	—	1
Total Cases	4	6	3	13

gery the combination of irradiation and sulfonamides was used in 24 cases with 11 fatalities, irradiation was given without sulfonamides in 11 cases with 1 death and sulfonamides were given without irradiation in 4 cases with 3 deaths. (Treatment and results are listed in Tables III A and B.)

It should be noted that during the period from 1934 to 1937 there were 3 patients who entered the hospital in extremis and during the period from 1937 to 1944, there were 4 patients who entered the hospital in extremis. Their condition was so critical that they would have died no matter what form of therapy was tried. Some died of other causes, such as fractured skull ruptured liver or spleen and carcinoma. Although these patients may have had a concomitant gas gangrene this was not the primary cause of death and therefore, their deaths should not be classified as gas-gangrene fatalities.

TABLE III B—TREATMENT AND RESULTS

(Forty two cases of gas gangrene seen at San Francisco City and County Hospital, during the period from 1937 to 1944)

Type of treatment	Recovered	Died	Died (Entered hospital in extremis)	Total
Surgery and serum	—	2	1	3
Surgery and radiation therapy	5	—	—	5
Surgery serum, and sulfonamides	1	3	—	4
Surgery serum, sulfonamides, and radiation therapy	11	6	2	19
Surgery serum, and radiation therapy	5	1	—	6
Surgery, sulfonamides, and radiation therapy	3	2	1	5
Total Cases	24	14	4	42
SUMMARY				
Total number of cases from 1934 to 1937	4	6	3	13
Total number of cases from 1937 to 1944	24	14	4	42
	18	30	7	55

DISCUSSION

The problem of gas gangrene remains unsolved. The incidence and mortality have not changed appreciably since World War I, despite the fact that during the interval between wars the potency of sera has been doubled and sulfonamide drugs have been introduced.

Authors are agreed on the fundamental principle that early adequate débridement must be done in order to prevent gas gangrene. Amputation continues to be one of the most effective methods of combating the disease. However this is indicated only when there is extensive tissue destruction or when the circulation is impaired or lost. Kelly believes that extensive débridement or amputation should not be done during the acute toxic phase of the disease.

Results obtained by the use of serum either as a prophylactic or therapeutic agent are confusing. Very few clinical series appear in the literature.

Clinical results before and since sulfonamide therapy came into common use do not substantiate the effectiveness of these drugs as suggested by experimental work. Of all the sulfonamides, sulfathiazole and sulfadiazine are most effective. However local use of the drugs has failed to lower the incidence of infection. The best results obtained thus far are reported by MacLennan; he cites a 30 per cent mortality. He believes the lowered mortality rate to be due to good surgery and intensive chemotherapy.

In experimental gas gangrene, penicillin (15-24) was found to be far superior to the sulfonamides. McKnight *et al* (31) report a case of gas gangrene treated with penicillin with excellent results, after all other methods had failed. However more experimental and clinical investigations are indicated before penicillin is universally adopted.

It is difficult to explain the poor results obtained with experimental irradiation as the results are good clinically. The mechanism of irradiation is not fully understood. Bisgard's conclusions merit serious consideration. He and his associates found the protective factor produced by irradiation to be highest after from twenty-four to forty-eight hours. He thinks that this protective agent is probably a proteolytic enzyme which is released when the highly sensitive leucocyte is subjected to irradiation. Results obtained in almost all inflammatory lesions confirm this experimental evidence, namely that most inflammations will respond to irradiation within from thirty-six to forty-eight hours.

Although it was rather difficult to evaluate the effectiveness of radiation therapy in percentages

because of the many variable factors involved—such as the different types of therapeutic measures and combinations of these measures used—it is the opinion of staff surgeons and radiologists that irradiation had been very beneficial and was a decided factor in both the lower mortality rate and the rapidity of recovery in the gas-gangrene cases treated at San Francisco County Hospital.

In some instances, response to irradiation was so dramatic that the surgeons insisted upon prophylactic irradiation for all compound fractures.

During the last few years, controversy has arisen regarding the combined use of sulfonamides and irradiation. Kelly and Dowell are of the opinion that they are antagonistic. Buschke and Cantil (6) in reporting on the treatment of post-operative parotitis, state that when sulfonamides and irradiation are used there is a decided increase in the number of cases with suppuration. It is impossible to evaluate accurately the use of sulfonamide therapy in the San Francisco County Hospital series because of the fact that many derivatives were used and these derivatives were often changed from day to day; in addition, there were intervals wherein no sulfonamides were used at all. However when sulfonamides were used, the dosages were adequate. In some cases, in spite of the intensive chemotherapy which was immediately given, gas gangrene was evident within from one to three days.

It is obvious that little progress has been made in eliminating this disease. Inasmuch as gas gangrene may increase in incidence as the allied armies advance on the Continent and in other theaters of the war we should work together for unification of therapy in the study of gas gangrene and thus benefit from our experiences and those of others.

The experiences of any one physician in treating gas gangrene are limited. Even in large institutions the number of cases seen is relatively small. However institutions in large cities, and at the present time medical organizations in the armed service forces, have an unparalleled opportunity to carry out a systematic investigation as to the relative values of the various therapeutic measures.

The following briefly outlined plan is suggested as an approach to the further over-all study of gas gangrene in an effort toward unification of the existing therapeutic measures. The ideal place for execution of such a plan might be in the armed services where the incidence of gas gangrene is higher than in civilian life.

It is recommended that a Central Committee composed of (1) a surgeon (2) a radiologist and

(3) a bacteriologist assign a course of treatment to several different hospital units. Within each hospital unit there could be a similar qualified Local Committee under direct supervision of the Central Committee. Inasmuch as adequate surgical débridement still remains the method of choice in combating this disease all units should have competent surgeons skilled in the art of débridement. In addition to the usual surgery one team could give all patients polyvalent serum in adequate doses (from 60,000 to 100,000 international units). A second team could use surgery, sulfanilamide crystals given locally (sulfanilamide is more soluble than sulfathiazole) and sulfathiazole given systemically. A third team could use surgery serum and sulfonamides. A fourth team could use surgery and penicillin. A fifth team could use surgery and radiation therapy. A sixth team, surgery, sulfathiazole, and irradiation and a seventh team surgery penicillin, and irradiation. It is obviously not necessary to stress the importance of supportive care no matter what method of therapy is attempted.

If such a plan were to become effective within a comparatively short time sufficient data could be collected and statistics compiled to evaluate properly the best method of treating gas gangrene. In all fairness to the patient, whether military or civilian gas gangrene should be treated in a thoroughly scientific manner.

SUMMARY

1. The incidence and mortality of gas gangrene have not shown any appreciable change since World War I.
2. The etiology is discussed.
3. The importance of early diagnosis and treatment of gas gangrene is reviewed.
4. Surgery still remains the choice therapeutic agent. However results obtained recently with irradiation and chemotherapy point to better results in the future provided closer co-operation is maintained between the surgeon radiologist and bacteriologist.
5. The results at the San Francisco County Hospital show a decided improvement with irradiation, and to a lesser extent, with the use of sulfonamides.
6. Prophylactic irradiation was given to 82 patients, of whom 2 developed gas gangrene and recovered with further irradiation. Although we may not draw definite conclusions from these figures, the future of prophylactic irradiation is thought-provoking.
7. A plan for the unification of therapeutic methods is suggested and briefly outlined.

The author wishes to express his sincere appreciation to Dr. R. R. Newell, Professor of Radiology Stanford University Medical School, for giving so generously of his wider experience, and for his guidance, criticisms, and thoughtful co-operation, in the preparation and completion of this study. He also wishes to thank Dr. T. E. Albers, Medical Superintendent, San Francisco County Hospital, for granting permission to review the medical records. (The cases used in this series were from both the Stanford Medical School and the University of California Medical School services at the San Francisco County Hospital. Many of these cases were given treatment by the author while he was on the Radiological Service at this hospital.)

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Johnstone, D. F.: Cavernous-Sinus Thrombosis Treated with Penicillin. *Lancet* Lond. 1945 248

Before the days of sulfathiazole and penicillin recovery from cavernous-sinus thrombosis was quite exceptional. This case report deals with a nineteen-year-old woman who recovered from this condition following treatment with penicillin. The original lesion was a small boil to the left of the tip of the nose which went on to edema of the nose, the forehead and both eyelids. She was admitted with a white count of 18,000 cells per cubic millimeter she was very sick and had a slight proptosis. She was put on doses of sulfathiazole 1 gm. every four hours. By the third day the temperature had fallen but her general condition had deteriorated she was comatose and had severe proptosis with papilledema of both eyes. After six days her condition still showed no improvement and penicillin was started. She was given a total of 500,000 units in three days and marked improvement was noted immediately although there was still swelling of the lids and both eyeballs were immobile. A blood culture was not taken.

She became somewhat drowsy and complained of headache and nausea, but there were no signs of meningitis and her white count was 10,000 per cubic millimeter. Ten days later penicillin was resumed and she was given 100,000 units twice a day for three days. There was an instant response and all her signs and symptoms disappeared except slight proptosis and occasional diplopia but the headache became more pronounced and a lumbar puncture was done which showed clear fluid under normal pressure and an occasional lymphocyte. An electroencephalogram was taken which showed a delta discharge in the left frontal lobe and as it was feared that she might have a left temporal lobe abscess an exploration of the left frontal lobe was done, but the result was negative. Recovery followed in a few weeks.

ADRIAN VERBROEGHEN M.D.

Penick, R. M., Jr.: Preauricular Sinusitis; Diagnosis and Treatment. *Semin. M J* 1945 38 103.

The congenital nature of preauricular sinuses is emphasized by a constant association with an external dimple which is present from birth. The presence of these epithelial sinuses is made evident only when infection supervenes. Then the clinical picture will depend largely upon the depth to which the preformed structure extends. The clinical course is variable. In some instances there are sharply defined episodes, in others there is chronic involvement accompanied by ulceration of the skin.



Fig. 1: The probe inserted in the external opening emerges where the abscess has broken through the skin behind the tragus.

The presence of the small congenital dimple or pit at the anterior edge of the ear is characteristic and should immediately suggest the diagnosis. The recurring nature should serve to differentiate it from tuberculous and fungus infections. Sebaceous cysts are frequently found behind the ear but rarely anterior to it.

Treatment consists in elimination of the infection first and excision of the epithelial lined tract afterward. The latter can usually be done under local anesthesia. A complete cure can be expected if all of the abnormal structure is removed.

NOAH D. FABRICANT M.D.

Ungley H. G. and Suggitt, S. C.: Fractures of the Zygomatic Tripod. *Brit J Surg.* 1944, 31 287

Fourteen cases of fracture of the zygomatic tripod are reported and some aspects of the clinical signs and symptoms, x ray findings, and treatment of these fractures are discussed. In all of these cases operations were performed either by the temporal or canine fossa approach. Inhalation anesthesia, administered by means of an intratracheal tube with oral pack was used in all cases. Local infiltration of the canine fossa was found to be a useful adjunct.

The clinical features of fracture of the zygomatic tripod are flattening of the facial contour palpable fracture line infraorbital nerve injury diplopia

hemorrhage into the maxillary sinus, unilateral epistaxis, surgical emphysema of the face, and difficulty in closing the jaws.

The most useful x ray view is the mentonasal, such as is used to demonstrate the auxiliary antra. The main points to note are the degree of comminution of the anterior wall of the antrum, the degree of impaction and telescoping of the zygoma into the cavity of the antrum, the associated opacity of the antrum, and the separation in the vicinity of the zygomaticofrontal or zygomaticotemporal synostosis.

The characteristics of the fracture vary according to the site and direction of the blow and may be classified into 3 groups. Blows from the front result in a double vertical fracture line, and cause the intervening block of bone to be driven directly backward. Blows from the anterolateral aspect are the more common and they cause the zygoma as a whole to be driven posteriorly and medially into the antrum, the fracture line passing through the weakest point, in the region of the intraorbital foramen. Blows from the nasal or anteromedial aspect, cause the anterolateral portion of the maxilla together with the zygoma to be driven backward and laterally and a large part of the orbital floor is carried in the same direction.

Prompt surgical treatment is indicated before the fractured fragments lose their mobility. Elevation by the temporal route has the advantage of a clean approach through an area removed from the site of injury but some fractures are not reducible by this method, or if the fragments are replaced they will not remain in position after the elevating force is removed, because of comminution of the bones, particularly of the wall of the antrum. A ray evidence of comminution of the anterior antral wall, or a long period of delay between the time of injury and operation contraindicates elevation by the temporal route. The canine-fossa approach has the advantage that the fracture is exposed to view and however great the impaction, deformity or comminution, reduction of the fragments can be achieved and maintained. It has the disadvantage of exposing the fracture through a potentially infected oral cavity, which makes it necessary to delay operation if dental sepsis is present. Fixation can be obtained by wiring, simple impaction, wedging with one of the loose bone fragments, or by the use of a bone graft. External fixation may also be used but was not found necessary in these cases.

JOHN L. LORQUET, M.D.

EYE

Blake, P. M. Injuries to the Eyes or to the Intracranial Visual Paths in Air Raid Casualties Admitted to Hospital. *Brit. J. Ophth.*, 1945, 29

Blake discusses injuries to the eyes and to the intracranial visual paths resulting from air raids in casualties admitted to hospitals and summarizes the findings as follows:

Of 8,833 persons exposed to within 100 feet of the explosion in 480 high-explosive bomb incidents, 0.75

per cent suffered injuries to the eyes or to the intracranial visual paths. Forty four per cent of the eye casualties lost the sight of one or both eyes or lost some vision. Eighty per cent of the eye casualties resulted from flying debris. Fifteen per cent of 66 casualties (10 individuals) in this series suffered from ocular injuries or injuries to the intracranial visual paths as a result of fractures of the vault of the skull or of the orbital bones. In this series of cases no eye injuries were caused by direct impact of the blast wave.

Direct injury to the eyes as well as fractures of the skull with consequent injury to the eye itself or to the intracranial visual pathways may result from bomb splinters, the flame of the explosion, secondary missiles (grit, sand, dust, and glass) and from direct injury by falls.

The actual number of serious eye injuries occurring at a distance of more than 100 feet from the fallen bomb was very small.

JOSUUA ZUCKERMAN, M.D.

Thorpe, H. E.: Nonmagnetic Intraocular Foreign Bodies. *J. Am. M. Ass.*, 1945, 27, 97

The author discusses the treatment of nonmagnetic intraocular foreign bodies. The increased employment of unskilled inexperienced personnel the accelerated industrial war effort the relative laxness in protective and preventive measures as well as the use of poorer quality hammers, chisels, and hatchets in civilian life has resulted in a larger number of nonmagnetic intraocular foreign-body cases in combat and in industry. Nonmagnetic foreign bodies comprise those made of manganese steel alloys, copper, brass, lead, aluminum, or wood. Magnetic foreign bodies can be differentiated from nonmagnetic by the history of injury examination of the working tools, examination of fragments removed from the face or other exposed parts of the body in explosion cases, and the use of the Berman locator. The Vogt and Comberg methods provide a simple x ray technique. Tridimensional concept of the foreign-body position is obtained with stereoscopic x-ray films and a localizing shell. Air injection in Tenon's space is of assistance in diagnosing double perforations.

Conservative therapy is advisable if more than three intraocular foreign bodies are present.

Prompt removal of intraocular foreign bodies with the aid of the endoscope is recommended. Groping in the vitreous with any instrument should be avoided.

The eyeball should never be mutilated simply to remove a chemically inert foreign body although glaucoma may be a later development in some of the cases.

Detachment of the retina should be treated.

The fellow eye should always be examined for the presence of another foreign body lodged after the same or a previous accident, and for the onset of sympathetic ophthalmia. To avoid infection it is necessary to remove foci of infection maintain asepsis and patency of the lacrimal passages, and to use foreign proteins and sulfonamide drugs.

JOSUUA ZUCKERMAN, M.D.

Cordes, F. C.: Metastatic Carcinoma of the Choroid. *Am. J. Ophth.*, 1944, 27, 1355

About 250 cases of metastatic carcinoma of the choroid have been reported in the literature, arising, in order of frequency from the breast, lungs and bronchial alimentary tract, prostate, and rarely from the thyroid, liver ovary and parotid gland. X ray therapy of the eye was reported three times with some improvement in vision but of course no effect upon the life expectancy of the patient.

A thirty-one year-old woman with bilateral metastasis to the choroid from a scirrhous carcinoma of the breast was seen by the author. One eye was enucleated and the diagnosis confirmed by microscopic examination. When the second eye became involved x-ray irradiation was employed. The tumor disappeared and left a lighter colored area in the fundus with fine dustlike clumpings of pigment and a suggested relative scotoma corresponding to the area. The central visual acuity remained 20/30. There was a recurrence of the tumor after fourteen months, with regression after further irradiation. The vision remained normal until the death of the patient, twenty three months after the first irradiation.

While the ultimate prognosis for life in these cases remains hopeless the use of radium or x rays on the metastatic growth in the eye may serve to retain useful vision for the patient, and should therefore be considered as a palliative measure. The earlier the choroidal metastasis is observed the better the chance of retaining useful vision by this means. It is of interest to note that although this patient received 3,315 roentgens at the time of the original irradiation and 3,356 roentgens at the time of the recurrence, no lens opacities had developed up to the time of death eight months after the second irradiation.

While the author believes radium or x rays will give identical results he prefers x rays because they can be given more readily and they are more universally available.

WILLIAM A. MAJOR, M.D.

EAR

Malone, P. W.: Aviation Deafness. *Arch. Otolaryng.*, 1944, 40, 468

The author reviews the basic experimental work on behavior of the eustachian tube during changes of altitude and presents personal observations showing the occurrence of a localized dip at the 4,000 frequency following two- and four hour flights in an open cockpit airplane. Such dips had disappeared

on the following day. In contrast, the result of repeated exposures is reflected in the audiogram of a pilot with 8,000 flying hours mostly in open cockpit planes which show a permanent hearing loss through the 1,000 to 4,000 frequencies. The use of a tight fitting helmet and headphones by the student in open cockpit planes prevented the localized hearing loss almost entirely. The permanent loss is regarded as being due to chronic accumulative fatigue of the end organ.

An audiogram is presented demonstrating the effect on the hearing of aviation pressure deafness or acute sero-otitis media. This produces a low tone deafness up to the frequency of 1,000 double vibrations in contrast to the deafness to noise which first appears at the 4,000 frequency.

JOHN R. LINDSAY, M.D.

NECK

Fox, J. R.: Paralysis of the Larynx; An Early Sign of Recurrence Following Radical Mastectomy for Carcinoma, with a Report of 6 Cases. *Arch. Surg.*, 1944, 49, 388.

When hoarseness occurs following mastectomy for carcinoma of the breast the possibility of metastasis must be considered. In each of the cases presented in this group there was a period following mastectomy during which the patient enjoyed complete symptomatic freedom from disease. This period varied from fourteen months to twelve years. The patient's well-being was then suddenly interrupted by changes in the voice, described as persistent hoarseness or huskiness. There were also intermittent weakness of the voice, a tendency for the voice to crack, and a nonproductive cough, unaccompanied by any evidence of infection of the respiratory tract. Dyspnea was severe in 1 patient and was experienced on exertion by the others. In each instance, however, it was the laryngeal disturbance which caused the patient to consult her physician.

Part of the drainage of lymph from the breast has been satisfactorily traced to the chain of nodes surrounding the recurrent laryngeal nerve. Metastasis, therefore, may be from a cancerous breast on the same or on the opposite side. There are three generally accepted lymphatic pathways of homolateral drainage which the author mentions.

Contralateral involvement, interestingly, is not the exception, since it occurs with almost the same frequency as paralysis of the same side.

Six cases are presented with the laryngeal findings.

JOHN F. DILLON, M.D.

SURGERY OF THE NERVOUS SYSTEM

PERIPHERAL NERVES

Holmes, W., Hight, W. B., and Seddon, H. P.: Ischemic Nerve Lesions Occurring in Volkmann Contracture. *Brit. J. Surg.* 1944, 31: 59.

Six cases of established Volkmann's contracture of an upper limb in which there was gross damage to the peripheral nerves from the ischemia were studied in detail and reported. This study was undertaken in an effort to determine the etiological part played by the nerve lesion in the deformity and whether or not the nerve lesion is amenable to treatment. In 4 of the 6 cases the radial pulse had been completely absent for a period varying from several hours to a week following the injury and much reduced in volume thereafter. In 1 additional case the arteriogram showed the site of arterial injury to be at the wrist, below the level at which the pulse is palpable. Oscillometer recordings demonstrated a serious impairment of the circulation below the level of the arterial injury and a slight reduction of oscillations immediately proximal to it.

Skin-temperature readings were of no value in the late differential diagnosis of ischemic contracture and peripheral nerve lesions since either a serious vascular lesion or a peripheral nerve lesion is sufficient to abolish reflex vasodilatation in the affected cutaneous zone. However skin temperature readings taken early after the onset of the lesion would differentiate a vascular from a nervous lesion since the denervated area would vasodilate. Only after an interval of about twenty-one days after denervation does the reflex vasodilatation fail to occur.

Arteriography in all cases gave a demonstrated obliteration of the main artery at the site of the injury with evidence of an established collateral circulation. The latter was sufficient to prevent gangrene; however there was a distinct deficiency of small vessels in the areas of muscular necrosis. These findings emphasize that Volkmann's paralysis is produced by damage to a main artery and the resulting widespread vascular spasm including even remote vessels. The vascular spasm included vessels proximal to the site of injury as well as distal to it.

Testing of electrical activity of the paralyzed muscles should easily distinguish between simple denervation and ischemic necrosis. The former gives the typical reaction of degeneration responses, while the latter fails to respond at all. However two major difficulties cause this method to fail in the differential diagnosis. Edema of the skin and subcutaneous tissues, often present in these deformities, causes percutaneous stimulation of muscle to be extremely unreliable. Also necrosis of muscle may be patchy and the response of non-necrotic parts to electrical stimulation might make it appear that the entire muscle was responding and was therefore unaffected by ischemia.

Three possible explanations of the extensive sensory and motor paralysis accompanying the muscular contracture are discussed: direct trauma to the nerves at the time of injury; nerve injury secondary to contracture of the muscles; and last, injury to the nerve caused by ischemia of the nerve itself. Pathological findings in the nerve trunks indicated to the authors that the latter mechanism was the cause of the nervous paralysis. The remarkable atrophy and induration of the main nerve trunks in the ischemic zone was quite unlike any condition seen after an uncomplicated nerve division or Wallerian degeneration. One case in which the ischemic zone did not extend to the most distal part of the limb, had markedly atrophic and fibrotic nerve trunks in the ischemic zone but more distally the trunks were of normal size and showed Wallerian degeneration.

Pathological study of the nerve trunks in the contracted limb revealed the nerve changes to vary from simple Wallerian change to complete destruction of all cells in the nerve. The latter nerve infarction is widely distributed in and near the necrotic muscle. Another ischemic change of great importance found was endoneurial collagenization. This is irreversible, and fiber regeneration through Schwann tubes obliterated by thickened endoneurial collagen is impossible.

In all of the cases reported in this article, there has been recovery in the radial muscles of the forearm except in distal muscles which were necrotic. Sensory and pseudomotor recovery had taken place in the distribution of the superficial radial nerve. Only little evidence of recovery in the median and ulnar nerves was noted. Thus it may be concluded that in severe cases of ischemic contracture there is not only a failure of recovery in the necrotic muscles, but likewise in muscles which are not necrotic but are supplied by nerves damaged by ischemia, and also that sensory recovery may be very imperfect. This failure of recovery is due to irreversible ischemic change in the nerves. There was no evidence from these cases that any form of treatment has any significant effect on the recovery of nerve function. The aim in dealing with Volkmann's contracture must be to prevent it.

HENRY A. SHENKIN, M.D.

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Shannon, E. W., and Morgan, C. W., Jr.: The Cerebrospinal-Fluid Protein in Metastatic Brain Tumors. *England J. M.* 1944, 311: 874.

Forty three cases of metastatic brain tumor have been studied with particular reference to the protein content of the cerebrospinal fluid. No constancy of the protein content was present, although almost all the cases show an increase above normal. In a com-

parison of the total protein content of the cerebrospinal fluid in primary brain tumors, no satisfactory differentiation could be perceived.

The conclusions resulting from this study were that the protein contents of the lumbar cerebrospinal fluid alone does not differentiate a metastatic neoplasm from a primary brain tumor.

HOWARD A. BROWN, M.D.

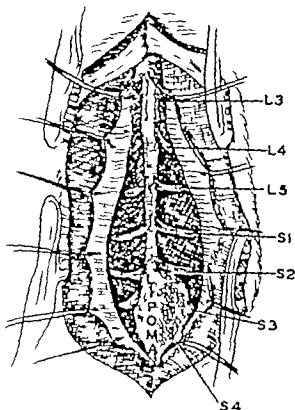


Fig. 2 Sketch of operative field to show the appearance of the caudal sac and its contents. The irregular spacing of the sacral roots which come off at right angles from the elongated conus medullaris is evident.

SPINAL CORD AND ITS COVERINGS

Walker, A. E.: Dilatation of the Vertebral Canal Associated with Congenital Anomalies of the Spinal Cord. *Am. J. Roentg.* 1944, 51: 571.

Four cases of dilatation of the spinal canal resulting from congenital anomalies of the spinal-cord structures have been reported. Three of these cases have been associated with myelodysplasia, and the fourth resulted from a vascular anomaly of the cord.

The dilatation of the canal has been discovered by roentgenograms in addition to the clinical neurological findings. The first 3 cases were in the lower portion of the spine and in the first instance the condition was associated with a lipomatous mass involving the nerve roots in the second, third, and fourth sacral root areas. The myelodysplastic condition found here consisted of a single trunk in the lumbosacral region from which the lumbar and sacral nerves were given off instead of a cauda equina. The sacral canal was markedly dilated and the condition was associated with a spina bifida occulta. The neu-



Fig. 1 Roentgenogram of the lumbosacral spine showing the enlargement of the spinal canal in the sacral region and the spina bifida occulta of the first sacral vertebra. The interpedicular distances measured: thoracic 1: 31 mm., 2: 23 mm., lumbar 3: 27 mm., 4: 28 mm., 5: 29 mm., 6: 31 mm., 7: 33 mm., and sacral 1: 42 mm.

rological symptoms consisted of mild impairment of the function of one lower extremity with urinary disturbances beginning in adolescence. The later symptoms were the result of tension upon the spinal cord associated with a greater growth of the vertebral column and relief was obtained by sectioning the adhesions binding the conus medullaris to the sacral sac.

The second case was associated with a splitting of the spinal cord in the upper lumbar region amounting to a diplomyelia or a diastematomyelia.

The third case was in the cervical spine with marked dilatation of the canal, and operation revealed a hydromyelia and diastematomyelia. In this case the choroid plexus was found to be in association with the cystic cavity which was encountered.

The final case was associated with deformity of the left foot, previously diagnosed as anterior poliomyelitis, and subsequent urinary difficulties in a fifteen-year-old boy. Bloody spinal fluid was encountered and x rays revealed marked widening of the lower thoracic and upper lumbar spinal canal. Operation revealed an angioma and an aneurysm of the spinal cord. Slow improvement followed.

The author believes that dilatation of the spinal canal as demonstrated by roentgenograms may indicate either a congenital anomaly or an erosion from tumor, but accurate differentiation is not possible by this means alone.

HOWARD A. BROWN, M.D.

Elliott, P. A. and Kramer, M.: Brachial Pain from Herniation of Cervical Intervertebral Disc. *Lancet*, Lond., 1945 248 4.

This article is from a military hospital for head injuries and concerns 8 cases of pain in the upper limb which, on clinical and radiological grounds, were thought to be due to herniation of the sixth cervical intervertebral disc. There was partial verification of 3 of the cases by a pantopaque myelogram. However none of the patients were operated on they were all treated by conservative management.

On the assumption that these were cases of herniated discs in the neck region the clinical findings were recorded. It was found for instance that neck movements to the side of the lesion aggravated the pain. The pain was accentuated by coughing and sneezing and at the same time it was relieved by mechanical traction on the head. In this series, most of the hypaesthesia and numbness was felt in the index finger and the thumb for in all of the cases in question it was presumed that the seventh cervical nerve root was affected. In 1 case there was pain on the inside of the hand and arm to the ring and little finger and this was thought to be due to secondary scalenus spasm. Trauma did not seem to be an essential part of the clinical picture. The uniform distribution of the pain was down the back of the shoulder down the back of the arm to the radial border of the forearm, and sometimes into the upper pectoral region. There was limitation of movement in the neck and the most constant reflex finding was a reduced or absent triceps jerk with hypaesthesia of the thumb and index finger. ADRIEN VERBOOGHEM M.D.

MISCELLANEOUS

Hamilton, J. E. Whitcomb, B. B. and Woodhall, B.: Penicillin in the Treatment of Surgical Infections of the Central Nervous System. *Surg Clin. N. America*, 1944, 24 1389.

Twelve cases of surgical infection of the central nervous system which have been treated by penicillin

are reported. These include 6 brain abscesses, 4 epidural abscesses, and 2 cases of traumatic meningitis. One patient succumbed and this was a case of brain abscess secondary to a suppuration of the lungs.

The authors stress the fact that penicillin passes through the choroid plexus into the cerebrospinal fluid only in minute traces, and certainly not in therapeutic amounts. Previous experimental studies by Pilcher have shown that the intravenous use of penicillin is ineffective in the treatment of staphylococcal and pneumococcal meningitis in dogs, whereas a marked beneficial effect resulted when the drug was administered intrathecally.

Further emphasis is laid upon the fact that adequate surgical treatment must be combined with proper dosage and administration of penicillin. In the case of brain abscess, improvement is noted during the early stage of cerebritis when penicillin is used parenterally. Once the abscess is formed, however penicillin is of little benefit unless it is used locally in the abscess cavity and when it is so used adequate dosages running up to 50,000 or more units, are necessary.

The removal of infected bone, or at least of sequestrae is a necessary adjunct if satisfactory results from the use of penicillin are to be expected.

One patient, who had evidence of brain abscess secondary to a lung abscess, has been reported as cured—which is unique as cases of this type have almost invariably been considered fatal in the past.

In meningitis, penicillin must be used intrathecally in order to obtain therapeutic effects in the subarachnoid system and dosages have averaged from 10,000 to 50,000 units daily. It has been shown that the therapeutic level of penicillin remains in the subarachnoid system as long as twenty-four hours after the injection of 10,000 units.

The lumbar route is advised for injection, with occasional use of the posterior cistern or even the ventricle in obstructive cases.

HOWARD A. BROWN M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Gershon-Cohen, J. and Dalbridge R. E.: Pseudarthrosis, Synchondrosis, and Other Anomalies of the First Ribs. *Am. J. Roentg.*, 1945 53 49.

During the course of routine roentgenological examinations of the chest many anomalies may be seen with or without pertinent symptomatology. It is important for the roentgenologist to be able to recognize anomalies that have no referable symptomatology as well as those that do.

Anomalies of the first rib occur most frequently and asymmetry or failure of ossification of the anterior aspect of the rib is observed most often. Failure of ossification according to Todd, is due to compression of the subclavian vessels during the embryological development. Bifid first ribs are rare. Some times the entire rib is absent.

Synchondrosis generally is seen in the posterior third of the rib. At times it is almost impossible to distinguish a synchondrosis from a pseudarthrosis. Absence of history of injury, no evidence of callus, smooth edges along the plane of dissolution, and no abnormal bone changes are in favor of a synchondrosis. Spontaneous rib fractures can occur with no history of injury. However in such instances some tenderness is present as well as a lump caused by callus formation. Pseudarthrosis may be due to muscle pull of the scalenus anticus. Bilateral fractures with resultant pseudarthrosis are rare.

Although most anomalies of the first rib are of no clinical significance, it is important to differentiate between a congenital synchondrosis and fracture pseudarthrosis.

MAURICE D. SACHS, M.D.

Graustman R. L., and Goldman M. L.: Tuberculous of the Breast. Report of 9 Cases Including 2 Cases of Coexisting Carcinoma and Tuberculous. *Am. J. Surg.* 1945 67 48.

Approximately 1 of every 100 breast conditions is tuberculous mastitis. The portal of entry of the tubercle bacillus is often difficult to determine. In various of the breast may occur by one of the following routes: through the milk ducts, by way of the nipple through abrasions of the skin by direct extension from the lungs and chest through the blood stream and through the lymphatics. In most cases, however the tubercle bacillus is carried to the breast by retrograde extension through the lymphatics from tuberculous cervical axillary or mediastinal lymph nodes. Trauma may be an etiological factor in rare instances.

In the series reported the average age of the patient was thirty-five years. Although pregnancy and lactation are predisposing factors in the etiology of tuberculosis of the breast, 30 per cent of the women with mammary tuberculosis were single, and approximately 4 per cent of all cases occurred in males.

For practical clinical purposes the disease is considered as being of 2 types—a primary type in which there is no demonstrable evidence of tuberculosis elsewhere in the body and a secondary type in which evidence of tuberculosis elsewhere is present.

Based on gross pathological findings the cases fall into 3 groups:

1. *Nodular* The tubercle, usually situated in the connective tissue enlarges to form a lump from 2 to 10 cm in diameter. As the condition progresses caseation and suppuration occur and sinus formation may develop.

2. *Sclerosing* This form of the disease is characterized by excess fibrosis and is seen more often in older people.

3. *Typical* This includes rare types of lesions such as obliterating mastitis and intraglandular cold abscess.

Most patients are in apparent good health. The earliest symptom is usually a painless lump in the breast. An early complaint is a discharging sinus (in from 20 to 30 per cent of cases). Enlarged axillary nodes are present in about half of the cases. The physical findings depend on the stage of the disease and the type of the underlying pathological condition.

A differential diagnosis is to be made from simple pyogenic mastitis, degenerated gumma, actinomycosis, and carcinoma. When no sinus formation is present, a differential diagnosis is to be made from carcinoma, benign fibroepithelial tumors, chronic cystic mastitis, gumma, plasma-cell mastitis and traumatic fat necrosis.

In primary cases the prognosis is good. In secondary cases the prognosis depends on the primary focus and its activity and extent. The generally accepted treatment of choice is excision.

Guinea-pig inoculation in addition to the usual bacteriological study of chronic discharging breast sinuses is advisable. For the proper surgical management of all suspicious breast lesions the use of the frozen section is essential. SAMUEL KADW M.D.

Adair F. B., and Herrmann J. B.: Primary Lymphosarcoma of the Breast. *Surgery* 1944, 16 836

The authors review the literature on primary lymphosarcoma of the breast, and conclude that only 3 of the reported cases satisfy their requirements for classification as localized primary lymphosarcoma of this organ.

In the past twenty years 445 patients with benign tumor and 650 patients with malignant tumor were seen on the breast service of the Memorial Hospital, New York, New York. There were only 5 cases of primary localized lymphosarcoma. The patients were white women in the fourth or fifth decade of life. The time which elapsed between the discovery of the tumor and the institution of sur-

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A differential diagnosis is to be made from simple pyogenic mastitis, degenerated gumma, actinomycosis, and carcinoma. When no sinus formation is present, a differential diagnosis is to be made from carcinoma, benign fibroepithelial tumors, chronic cystic mastitis, gumma, plasma-cell mastitis and traumatic fat necrosis.

In primary cases the prognosis is good. In secondary cases the prognosis depends on the primary focus and its activity and extent. The generally accepted treatment of choice is excision.

Guinea pig inoculation in addition to the usual bacteriological study of chronic discharging breast sinuses, is advisable. For the proper surgical management of all suspicious breast lesions the use of the frozen section is essential. SAMUEL KAHN, M.D.

Adair, F. E., and Herrmann, J. B.: Primary Lymphosarcoma of the Breast. *Surgery* 1944, 16 836.

The authors review the literature on primary lymphosarcoma of the breast, and conclude that only 2 of the reported cases satisfy their requirements for classification as localized primary lymphosarcoma of this organ.

In the past twenty years, 4,415 patients with benign tumor and 6,519 patients with malignant tumor were seen on the breast service of the Memorial Hospital, New York, New York. There were only 5 cases of primary localized lymphosarcoma. The patients were white women in the fourth or fifth decade of life. The time which elapsed between the discovery of the tumor and the institution of sur-

gery was from two to four weeks. The right breast was involved in 4 of the 5 patients. The lesion was single in 4 patients, and in 1 patient there were 2 lesions. The lesion was located in the upper and outer quadrant of the breast in 4 of the 5 cases. The tumor mass ranged from 1 to 4 cm in diameter. In 1 case there was nipple retraction, and in 3 skin attachment or dimpling. X-ray examination of the chest in 3 cases revealed an absence of pulmonary or mediastinal involvement.

All the patients except the one who had undergone a local excision of the tumor elsewhere were treated by surgery alone. Radical mastectomy was performed in 3 cases, and a simple mastectomy with axillary dissection was done in the fourth case. The patient who had a local excision of the tumor elsewhere was given high-voltage irradiation to the area of excision but not to the axilla.

The pathological diagnosis in 3 cases was reticulocell sarcoma, and in 1 case, follicular lymphosarcoma (Brill Symmers disease). The section of the tumor excised elsewhere was interpreted as consistent with lymphosarcoma. No involvement of the axillary nodes was found in any patient.

The 3 patients treated by radical mastectomy are alive and free of disease after periods of seven years, three years and six months, respectively. The patient treated by local excision and deep x-ray therapy is also alive and free of disease one and one half years after the surgical procedure. The patient treated by simple mastectomy is alive three months following surgery.

For O. L. TINKER, M.D.

HEART AND PERICARDIUM

Cooper, F. W., Stead, E. A., and Warren, J. V.: The Beneficial Effect of Intravenous Infusions in Acute Pericardial Tamponade. *Ann. Surg.* 944, 20-8.

Opinions differ as to whether or not the intravenous administration of physiological saline solution is beneficial in patients with acute pericardial tamponade resulting from a stab wound of the heart or great vessels. The elevated venous pressure in pericardial tamponade is said to be produced by the damming up of blood due to obstruction to the venous inflow to the heart. When the venous pressure exceeds the pressure of the obstruction the blood can flow into the heart. Thus, survival in pericardial tamponade is dependent upon elevation of the venous pressure. This rise in venous pressure is produced by a combination of vasoconstriction and redistribution of blood in the vascular system. Because the venous inflow to the heart is then dependent on the cardiac output, the amount of venous distention which can be caused by damming up the venous inflow to the heart is limited by the diminished cardiac output and venous filling. These experiments were undertaken to determine whether or not increase of the blood volume with intravenous fluids to raise the venous pressure might be beneficial in pericardial tamponade.

Acute pericardial tamponade was produced in 5 dogs by introducing physiological saline solution from a reservoir into the closed pericardial sac. The pressure required to produce severe symptoms varied in different animals from 12 to 22 cm. of water but it was quite constant for the same animal. After the pericardial pressure necessary to produce severe symptoms was determined, a rapid intravenous infusion was given to increase the blood volume. The dogs were then again subjected to pericardial tamponade and it was found that they could withstand from 92 to 146 per cent greater pressure. Two experiments were conducted with a closed system to duplicate the conditions of pericardial tamponade in human patients. Severe tamponade was produced and the tube leading from the pericardium was clamped. In both of these dogs there was distinct improvement with the intravenous administration of 300 cc. of saline solution.

From a theoretical standpoint, it appears that improvement in the circulation under these circumstances would depend upon the ability of the pericardium to stretch and allow an adequate cardiac filling with the increased venous pressure. In these experiments such stretching appeared to occur and the increased pericardial pressure was more than compensated for by the increased venous pressure.

Saline infusions were administered to 3 patients admitted to the hospital with traumatic pericardial tamponade, and in each case the arterial pressure rose and the patient became more rational. At operation the wounds in the heart and pericardium were found to have remained sealed, in spite of the rise of arterial pressure. This form of therapy may serve as a useful adjunct in the treatment of pericardial tamponade either by aspiration or operation, and in certain selected patients may restore the circulation to an adequate level without aspiration or operation.

JOHN L. LINQVIST, M.D.

ESOPHAGUS AND MEDIASTINUM

Clark, D. E.: Trans thoracic Esophagogastrostomy for Carcinoma of the Middle Third of the Esophagus. Report of a Successful Resection. *J. Surg.* 945, 3-65.

Trans thoracic resection for carcinoma of the lower third of the esophagus with esophagogastrostomy has become a well standardized procedure which can be performed with considerable success.

Progress in the surgical treatment for carcinoma of the middle third of the esophagus has not kept pace with that of the lower third or with other thoracic tumors. Until recently all of the carcinomas of the middle third were resected by the method used and developed by Torek. Although this procedure fulfills the principles of good cancer surgery it is not entirely satisfactory, in that esophagogastric continuity is not re-established.

The cervical esophagostomy may be connected to the abdominal esophagostomy or gastrostomy by means of an anterior thoracic esophagoplasty or if

such is unsuccessful, a rubber tube. The rubber tube connection is an unending source of complaints. The tube frequently becomes dislodged or plugged and is almost constantly leaking. Many ingenious methods have been proposed for anterior thoracic esophagoplasty utilizing skin tubes, stomach, gastric tube, jejunum colon, and a combination of jejunum and skin tube. Most of these operations require multiple operative procedures and are quite difficult to perform. Fifty-eight cases were operated upon by Ludwig by the combined methods. He used a segment of jejunum for the lower part and a skin tube above.

Construction of skin tubes either with or without jejunal transplantation usually requires numerous operative procedures. Fistulas develop and strictures occur at the mucocutaneous junctions. Both of these distressing complications are difficult to handle. More than 50 per cent of anterior dermatoesophagoplasties are never completed. Most of the patients dying of recurrence before the skin tube is completed.

Recently Garlock described a method for reestablishment of esophagogastric continuity after resection of a carcinoma of the middle third of the esophagus. In his case he anastomosed the fundus of the stomach over and above the arch of the aorta. This procedure is a definite advance in the surgical treatment of carcinoma of the middle third of the esophagus. It not only affords radical removal of the tumor but eliminates artificial swallowing devices and anterior thoracic esophagoplasties. The success of Garlock prompted the author to employ a similar procedure in a man who had a carcinoma involving the middle and lower thirds of the esophagus.

For the sake of brevity only the most salient points are mentioned here. Under positive pressure ethylene-oxygen-ether anesthesia, a long incision was made over the course of the seventh rib beginning at the costochondral junction anteriorly and extending backward to about the lateral edge of the recti-spinae muscles. At this level it was carried upward for a distance of about 8 cm. The entire seventh rib was removed subperiosteally and the fifth, sixth, eighth, and ninth ribs were transected. The phrenic nerve was crushed just above the diaphragm. The mediastinal pleura was incised along the medial edge of the aorta from the diaphragm to the arch of the aorta. By means of blunt and sharp dissection the esophagus was mobilized from the posterior mediastinum. Both vagus nerves were divided above the diaphragm. The mediastinal pleura was incised above the arch to the supra-sternal notch. The esophagus above the level of the tumor was easily freed. By careful blunt dissection the involved esophagus was freed from beneath the arch of the aorta and from the trachea and left main bronchus. A 16-cm. radial incision was made in the diaphragm from the periphery toward the esophageal hiatus. The left phrenic artery was divided and ligated. The greater omentum was divided close to the stomach down to near the pylorus. This divi-

sion was made so that the gastro-epiploic vessels remained in the omentum. The ligation was carried down to where the first branch of the right gastro-epiploic artery came off to the stomach. In order to remove the lymph node metastases it was necessary to divide the left gastric artery near the celiac axis. The upper and lower branches of the left gastric artery were divided and the gastrohepatic omentum incised near the liver. The lesser omentum, the left gastric artery and the accompanying nodes of the latter were completely excised from the lesser curvature of the stomach. The stomach was divided just below the cardioesophageal junction and the distal end infolded with two rows of linen sutures. The proximal end was covered with a rubber glove. The mobilized esophagus was then drawn out through the opening in the mediastinal pleura above and to the left of the arch of the aorta. The stomach, which appeared viable, was easily brought up into the chest and an anastomosis made between the end of the esophagus and an opening in the fundus of the stomach. The first posterior row of sutures was placed about 6 cm. above the upper limits of the tumor. An umbilical tape was placed around the esophagus 3 cm. above these sutures and tied twice the second tie being a slipknot. The lower two-thirds of the esophagus was now removed and the anastomosis completed. The elongated stomach was sutured to the pericardium and pleura over the aorta as far as the diaphragm which was closed with interrupted sutures around the prepyloric portion of the stomach. Five grams of sulfathiazole crystals were sprinkled in the operative field. A de Pezzer catheter was inserted posterolaterally through the ninth interspace for pleural drainage.

The patient's postoperative course was complicated by a chylothorax. Because of the anatomic location of the thoracic duct, the injury of it may be more frequent in resecting lesions of the middle third of the esophagus than in operations for lesions of the lower third. Since the protein content of chyle is from 2 to 4 gm. per cent depletion of the protein stores will occur very rapidly unless adequate replacement is promptly instituted. Plasma should be given or the chylous fluid if sterile may be administered intravenously.

Roentgenological study after the ingestion of barium, made about four months after the operation revealed a marked obstruction of the stomach where it passed through the diaphragm. The excursion of the left leaf of the diaphragm was full. It appeared that the obstruction was due to regeneration of the phrenic nerve and recovery of the muscle tone of the diaphragm. In view of this, it is a question if it would not be better to excise a long segment of the phrenic nerve to insure permanent paralysis of the left leaf of the diaphragm.

The patient got along quite well for three and one-half months, then he began to lose weight and strength. A cough developed and his appetite failed. His condition gradually became worse and he died five months after the operation.

In the author's case the greater and lesser curvatures were ligated to the prepyloric region and only the blood supply which comes from the prepyloric segments of the right gastric and right gastroepiploic arteries was left. Despite this extensive sacrifice of blood vessels the circulation of the stomach remained adequate.

Ligation of the blood supply to such an extent presumably may result in necrosis of the stomach in some cases. Therefore, a safer procedure would be to leave the right and left gastroepiploic vessels attached to the stomach, and divide and ligate the omentum distally. If this were done, complete removal of the left gastric artery and its accompanying nodes could be performed with very little fear of impairment of the gastric circulation. Since the lymph nodes along the lesser curvature of the stomach are intimately associated with the lymphatic drainage of the esophagus, and usually contain metastases, their removal is definitely indicated.

JOSEPH K. NARAT, M.D.

MISCELLANEOUS

Barrett, N. R.: Hemothorax; Notes and Observations. *Lancet*, Lond., 1945 248 3

Hemothorax comprehends the chief part of traumatic thoracic surgery. The author's notes are based upon experience gathered at the thoracic surgical unit of a war hospital and at a coast hospital.

Hemothorax has 3 immediate harmful effects—blood loss, pleural cavitation, and the development of a space-occupying lesion in the chest. In some cases the blood is absorbed spontaneously with no residual effects, but more generally the bloody effusion acts as a retained foreign body and pathological changes continue. Fibrin is laid down and this forms localized pockets, as well as an envelope around the lung. The fibrin layer on the lung prevents re-expansion, and healing results in contractures of the chest wall, diaphragm or mediastinum.

The bleeding may come from the lung or the parietes. Bleeding from the lung may be profuse, but it is usually short-lived. Persistent or delayed bleeding is generally due to wounds involving the chest wall or diaphragm. The diagnosis is usually not difficult, but can be confused with atelectasis or diaphragmatic hernia. In the absence of pleural adhesions, shifting of the mediastinum is a late sign and indicates extensive bleeding. In a case of moderate bleeding with mediastinal shift, the lung is probably held out by pre-existing adhesions. Common symptoms are shock, pain, dyspnea, and fever.

The treatment is varied, but the author bases his therapy on the basis that (1) total expansion of the lung should be obtained at the earliest possible moment (2) a hemothorax is a foreign body in a vital serous cavity, (3) there is no way of predicting in which cases the blood will not be absorbed (4) infection may occur at any time, and (5) there is little hemostatic value in leaving the blood in situ, and aspiration is likely to start a fresh hemorrhage only

if a high negative pressure is produced. Repeated aspirations may be very effective if started within twenty-four hours. In many cases this is the only therapy needed. If hemorrhage is still going on the patient should be given a transfusion and the bleeding point secured by operation. If bleeding has stopped, but a massive hemothorax is present and cannot be emptied by aspiration, a thoracoscopic aspiration may be done. If the hemothorax has clotted or bleeding persists for weeks, the chest should be opened the pleura emptied, and decortication of the lung performed. If a foreign body of considerable size is present in addition to the hematoma, a thoracotomy is done. In cases of combined thoracoabdominal wounds care should be taken not to overlook a hemothorax. THOMAS F. THORNTON, JR., M.D.

Coleman, F. P.: Traumatic Hemothorax; Decortication in the Treatment of the Chronic Uninfected Type. *Arch. Surg.* 1945, 50 14.

The respiratory disability associated with the later stages of wounds of the thorax incurred during war is a real problem. Infection is primarily responsible for the disability in the majority of cases, however or ganization of blood within the pleural cavity untended by sepsis is not uncommon and often leads to an even greater degree of respiratory invalidism.

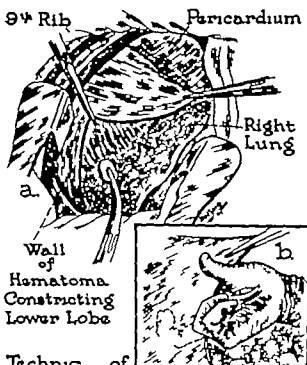
When blood escapes into the pleural cavity it apparently undergoes early formation of a clot. The views expressed by Elliott offer an explanation for what appears to be the absence of clotting of blood within the pleural cavity. The author stated that the effused blood very rapidly passes through the clotting process, but that the coagulation is interfered with by the respiratory movements so that the fibrin is to a considerable extent whipped out of the blood. If bleeding into the pleural cavity is slow the blood is readily deprived of fibrin by the movements of the diaphragm and the heart. The pleura is irritated by the blood, and an effusion is poured out. The blood free of fibrin mixes with the effusion, resulting in a fluid hemothorax, which does not undergo formation of a clot on removal from the pleural cavity. The fibrin is usually deposited in a dependent location. If bleeding into the pleural cavity is rapid, sufficient agitation may not be present to bring about defibrination of the blood, and a solid hemothorax results. Other factors which favor formation of a massive clot within the thorax are extensive destruction of tissue and retention of foreign bodies within the pleural cavity.

The pleura is able to cope with the deposit of fibrin in a small hemothorax. The associated effusion is either aspirated or absorbed. In such cases no functional incapacity results. On the other hand, deposition of fibrin accompanied by a process of organization may be sufficient to lead to the formation of dense pleural adhesions. The mobility of the diaphragm, thoracic wall, and lung is restricted. In such cases a routine roentgen film may reveal only slight haziness over the base of the lung, however the limitation of the motion of the diaphragm is readily ob-

vious during fluoroscopy and a deposit of fibrin may be identified in the costovertebral sulcus by suitable lateral roentgenograms of the chest. The mechanism of the disability associated with the organization of a large hematoma within the pleural cavity is obvious. The thick wall of the hematoma fixes the pleural surface of the ribs, and thereby interferes with the normal widening of the intercostal spaces during inspiration. Organized fibrous tissue contracts, drawing the ribs closer together and the normal longitudinal curves of the ribs are lost. The involved hemithorax becomes flattened and immobile. The diaphragm, when involved loses its function entirely. The involved portion of the lung is usually normal but it cannot perform its function when it is confined in a fibrous encasement.

The temporary disability associated with uncomplicated hemithorax has been attributed to the organization of fibrin within the pleural cavity. Pain and shortness of breath are the primary symptomatic manifestations. Detailed roentgenograms and fluoroscopic examination of the chest, as a rule, reveal some fixation of the diaphragm and a deposit of fibrin in the costovertebral gutter. The symptomatic manifestations and the disability associated with obvious chronic organized hemithorax do not require a great deal of comment. Patients with this complication are unfit for military duty. They are chronic invalids. A low-grade fever is usually present, and even in the absence of infection the temperature may reach a daily level as high as 102 F. There is distinct pallor to the skin and frequently secondary anemia is present. Dyspnea on exertion and pain in the involved side of the chest are common symptoms. The hemithorax is flattened and immobile. There is compensatory emphysema of the uninvolved lung. The compensatory activity of the contralateral lung exaggerates the deformity produced by the chronic organized hemithorax. In the treatment of chronic traumatic uninfected hemithorax the surgical approach is governed somewhat by the site of the formation of the clot. The blood clot usually assumes a dependent position within the pleural cavity lying in the costovertebral gutter and overlying the diaphragm.

Access to this region is readily accomplished by making a posterolateral incision and the pleural cavity is entered through the seventh or eighth intercostal space. The wall of the hematoma is encountered on division of the intercostal muscles and the parietal pleura. A cleavage plane between the wall of the hematoma and the pleura may be developed with ease, because of the fact that these structures are bound together by only a light net work of vascular and fibrous tissue. The wall of the hematoma is freed from the adjacent structures by blunt dissection the surgeon working away from the thoracic wall and lung. The index finger or a blunt gauze dissector has proved satisfactory for this procedure. It is possible to mobilize a large hematoma in this manner without disruption of its physical characteristics. After the lung, the diaphragm and



Technic of Decortication of Lower Lobe

Fig. 1. Illustrations of the operative procedure.

the thoracic wall have been freed of the hematoma, the underlying pleura may be observed to be practically normal. It is not thickened and it still has a somewhat smooth and glistening appearance. The previously constricted diaphragm and lung will function in a normal manner with removal of the fibrous encasement. In a clotted hemithorax of less than three weeks' duration the cleavage plane between the pleura and the wall of the hematoma is not sharply demarcated. At this stage the wall of the hematoma has not become well organized and there is persistence of the edema of the adjacent pleura. Early removal of the deposit of fibrin does not permit the ready re-expansion of the lung which is so admirably demonstrated when this structure is freed of a well organized hematoma. BENJAMIN GOLDMAN M.D.

Johnson, E. K., Wolff W. L., and Lambert, A. V. S.: Sulfonamide Therapy in Clean Thoracoplasty Cases. *Ann. Surg.* 1945 121: 120.

The authors report concerns 83 patients who were subjected to 303 clean thoracoplasty operations. The modern thoracoplasty operation averaging 3 ribs at each stage was performed in almost every case and generally silk technique was used. There were 3 series of operations (1) those done after sulfonamides were applied locally (2) those done after sulfonamides were given orally and those done on patients who had received no sulfonamides (controls).

The first series consisted of 97 operations, done after the sulfonamides were applied locally to the thoracoplasty wounds, an average of 4.7 gm. being

used per operation. No known toxic reactions occurred and there was no evidence of delayed wound healing. Twenty of the 97 cases were reviewed to determine the excess wound fluid and an average of 328 cc. was aspirated from each. Blood and wound fluid levels were found to be between 3.0 and 5.0 mgm. per cent within eight hours. The blood level was down in forty-eight hours and the wound fluid level was down in ninety-two hours. The sulfadiazine levels rose and fell less rapidly than the sulfanilamide levels.

The second series numbered 39 operations, after which the patients received sulfonamides orally for three or four days. There were 4 reactions. All wounds healed by the tenth postoperative day. Six of 10 cases analyzed for excess wound fluid were found to have about 135 cc. each. Levels from 5.0 to 9.0 mgm. per cent were present in both the blood and wound fluid while the drug was given. The wound fluid level was usually slightly higher. Sulfadiazine levels lagged as in the first series.

The third series was composed of 67 operations which were not accompanied by sulfonamide therapy. All wounds healed promptly. Fifteen cases

were examined for excess wound fluid serum, and in the 8 cases which developed excess serum it averaged 110 cc.

Delay in healing was not noted in the 3 series, although excess fluid was more likely to form if the sulfonamides were applied locally.

The incidence of pyogenic infections in the entire series was 5.4 per cent. All bacterial contaminants were cocci. There was no great difference between the controls and the treated cases.

It does not appear logical to subject clean thoracoplasty wounds to routine prophylactic sulfonamide therapy as only a small portion become contaminated and even a smaller number develop infections. The occurrence of excessive wound fluid with the local application and the occasional toxic reaction with the oral administration of sulfonamide therapy seem more hazardous than the infrequent severe infections. If contamination of the thoracoplasty wound is indicated by cultures the authors suggest the systemic use of sulfonamides. If gross contamination is present local plus systemic therapy may be employed.

THOMAS F. THORNTON, J. M.D.

SURGERY OF THE ABDOMEN

ABDOMINAL WALL AND PERITONEUM

Narando, M M Pierson J C. McNeer G and Pack, G T: *The Economic Value of Peritoneoscopy* Ann Surg 1945 131 185

Peritoneoscopy as a diagnostic procedure has been known to clinicians since 1901

At the Memorial Hospital, New York the chief interest in this field has been in the determination or recognition of the inoperability of various intra abdominal neoplasms. One can frequently appreciate the inoperability of some cancers by this examination, but on the contrary the resectability can never be ascertained with any degree of certainty. If this fact were universally known the limitations of the instrument would be accepted and no extravagant claims for its use would be made. The recognition of metastases in the liver or carcinomatous implants on the parietal or pelvic peritoneum for example, would discourage any surgical attempt at removal of a gastric cancer.

The chief indication for its use is the attempted determination of inoperability in borderline cases when clinical evidence of such inoperability does not exist. If the criteria which determine inoperability are not fulfilled on peritoneoscopic study a celotomy should be done immediately and the tumor will then be found to be resectable or inoperable. This discovery of inoperability should not be listed as a failure for peritoneoscopy because it only confirms the well recognized limitations and handicaps of the method.

This relatively safe minor procedure will often prevent useless exploratory celotomies in patients who are poor surgical risks. The economic advantages to the patient and to the hospital are great.

Peritoneoscopy is generally indicated in the following conditions: intra abdominal tumors, particularly malignant tumors; cirrhosis of the liver; ascites of undetermined origin; tuberculous peritonitis; ectopic pregnancy; and lesions of the internal female genitalia. The procedure is contraindicated in acute inflammatory conditions of the abdomen; advanced cardiac or pulmonary diseases; and extensive peritoneal adhesions. The single death in this series occurred in a jaundiced patient.

Since January 1940 peritoneoscopy was employed upon 80 patients at the Memorial Hospital. Of these 26 had primary gastric cancers, 12 had cirrhosis of the liver, 7 had neoplasms of the gall bladder or liver and 6 patients with mammary cancer had peritoneoscopic visualization of their livers.

Of the 26 patients with carcinoma of the stomach who were subjected to peritoneoscopy the purpose of peritoneoscopy was satisfactorily fulfilled in 14 or 53.8 per cent. In 7 patients, metastatic cancer was found to involve the liver, parietal peritoneum or both, and in this group a major operation was

avoided. In 7 other patients whose gastric cancers were at first thought to be of questionable or borderline resectability the endoscopic findings did not contraindicate surgical exploration, which was undertaken and the cancers were removed. In 12 patients (46.1 per cent) the procedure was of little value.

Peritoneoscopy is of great value in the differential diagnosis between cirrhosis and malignant tumors involving the liver. In 9 of a group of 12 cases exploratory celotomy was avoided because of the fact that the correct diagnosis was easily established on peritoneoscopy.

HARRY W. FINE, M.D.

GASTROINTESTINAL TRACT

Saunders, W W: *Gastric Herniation at the Esophageal Hiatus. Permanent Foundation M. Eull* 945 1 1

Herniation of the stomach at the esophageal hiatus is the most frequent type of diaphragmatic hernia. As a rule it is incidental and symptomless but it may cause serious or even fatal bleeding ulceration with perforation, distressing nausea and vomiting as well as many other lesser complaints. The diagnosis of hiatus hernia may be suspected clinically when a patient complains of anginal pain worse after eating or when lying down in addition to other upper gastrointestinal symptoms. A ray study will usually show the lesion provided the proper supplemental maneuvers are utilized. These are roentgen examination of patients in the standing, supine, prone, and right oblique prone positions, with barium suspension in the esophagus. If this is not done some of the hernias which are reducible may be missed.

The type of hernia should be noted for the guidance of the surgeon who may undertake repair. If the esophagus is filled with barium mixture at the same time that the hernia is the relationship may be determined with the patient in one of the prone oblique positions. It is important to recognize those few cases in which the downward growth of the esophagus has not kept up with the caudal migration of the diaphragm because this forces a portion of the stomach to remain intrathoracic. These are not true hernias and should not be erroneously included in this group.

Of the 200 upper gastrointestinal examinations made during the past two years, 28 were found to be gastric hernias through the esophageal hiatus. In 20 of these 28 patients, the symptomatology could be explained only by the hiatus hernia, no other lesions being demonstrable. Nine of the patients had hernias which involved one third of the stomach, all the rest being small.

The often noted fact that size does not determine the presence or intensity of symptomatology held for this series, for 2 of the 4 patients without symptoms

had large herniations. In addition 80 per cent of these patients could be relieved by medical treatment and about 10 per cent had severe symptomatology which may require surgical intervention. The remaining 10 per cent had no symptomatology at all.

SAMUEL J. FOOTELOW M.D.

Fresman, H.: A Gastroscopic Control of the Treatment of Gastric Ulcer by Duodenal Feeding. *Brit. J. Surg.* 1944, 32, 3, 3.

The author makes a renewed attempt to popularize the method originally advocated and practiced by Einhorn in America and Ernest Young in London and consisting of duodenal feedings in order to provide a complete rest for the stomach and to limit its secretion to a minimum. Although roentgenography is still the standard method of choice in the diagnosis of an ulcer the author has found a number of ulcers on gastroscopy which were missed by the radiologist. This may have been accounted for by failure of the barium to fill the crater because the flow was already filled with slough of the mucus. Therefore, patients who present ulcer symptoms and in whom a negative x ray examination has been reported should be examined with the gastroscope, and the examination should be repeated subsequently before cessation of treatment is contemplated.

In 15 patients in whom duodenal feeding was carried out the average time required for healing was four weeks. This was confirmed gastroscopically. The types of chronic ulcer which respond most readily to the regime of duodenal feeding are (a) those of moderate or long duration without complications, (b) ulcers which have given rise to occasional hematemesis, and (c) early cases of penetrating ulcer.

Failures are usually due to (1) lack of co-operation by the patient, especially in the early stages of treatment. This lack of co-operation often includes surreptitious feedings (foods brought by relatives who believe they are being kind to the patient) (2) deep penetration into the pancreas and (3) an incorrect diagnosis, i.e., malignant ulcer or early malignant change in a chronic ulcer.

There is, of course, no direct evidence that duodenal feeding provides for a more permanent cure than when other methods of treatment are used but a breakdown of the old ulcer is far less likely because of the rapidity with which the original lesion heals under conditions in which this treatment is carried out.

It is advisable to keep the patient in bed for the first fortnight after treatment is begun. After this interval he is allowed up gradually. Many patients have carried on their work during treatment by duodenal feeding. Pain is absent in almost all cases within forty-eight hours of the start of the tube feedings. Rarely it may be necessary to give atropine hypodermically. If, however, pain persists after this short period, the diagnosis should be reviewed, for the possibility of deep penetration into the pancreas or malignant change in the ulcer must be considered.

As to the technique, preferably an Einhorn or Kyle's thin rubber tube No. 7 should be used. These two types are softer and more flexible than other types and are therefore less liable to irritate the pharynx. The tube is passed in the morning on a fasting stomach. It is proved to be in the duodenum if on attempting to aspirate with an attached hypodermic syringe, withdrawal of the plunger is difficult and the tube collapses as long as the withdrawal of fluid is easy. The tube still lies in the stomach. A glass container into which the food is placed is hung 3 ft. above the level of the head of the bed. To it are connected a rubber tube and a funnel, the distal end of the tube being connected by a glass tube to the duodenal tube. The following points should be observed: (a) the feeding should take from twenty to thirty minutes; (b) all food must be strained through gauze and given slightly warm; (c) before and after feedings a 10-cc. syringe of water followed by a syringe of air must be passed down the tube to keep it clear; (d) after feeding, the duodenal tube is disconnected, looped so as to occlude it, and fixed behind the patient's ear (A small spigot may be put in the end of the tube.); (e) the feeding apparatus must be cleansed with cold water after each feeding. The tube is retained for twenty-one days, it is then withdrawn and the patient is examined with the gastroscope. If healing is complete, the 'initial diet' is started; if not, the tube is replaced.

Nothing whatever enters the stomach. All food and medicine pass straight into the duodenum. Each feeding consists of 8 oz. of milk (dried milk can be used) plus any other substance such as arrowroot, eggs (or dried eggs) and lactose. Some patients cannot tolerate quite all of this quantity which is reduced accordingly. Seven feedings are given daily at two-hourly intervals, starting at 8 a.m. It is a good plan to alternate the preparations used in conjunction with milk. If constipation is present a suitable dose of cascara evacuant is given in the feeding. Vitamin C (ascorbic acid) 150 mgm. daily should also be added.

In very nervous patients a mixture of bromide and valerian given through the tube helps to allay any anxiety or mental stress, conditions which so very often accompany peptic ulceration. Occasionally excessive salivation may render the tube intolerable under these circumstances a hypodermic injection of atropine (gr. 1/50) once daily will overcome this difficulty.

The initial diet to follow the duodenal feeding immediately consists of a scrambled egg (or dried substitute) with toast and a little butter and a cupful of weak tea, with or without milk, but no sugar. For breakfast flaked boiled fish, sieved potatoes, and toast for lunch 2 teacupfuls of tea without sugar and a few plain biscuits in the afternoon and breast of chicken or rabbit, sieved potatoes, toast, junket, stewed prunes (sieved) and not more than ½ a tumblerful of water for supper. One hour before breakfast and lunch and on retiring, a tumbler

ful of hot water is offered. A gradual increase in the above diet is made until lean beef mutton, and other meat are included. No change in vegetables, however, should be made until two months have elapsed since the beginning of the treatment.

JOSEPH K. NARAT, M.D.

Carlaw, J.: Peptic Ulcer; A Study of the Number of Cases Treated in the Western Infirmary of Glasgow during Forty-Six years (1897 to 1942). *Glasgow M. J.*, 1944, 142: 183

In the last twenty years there has been an alarming increase of peptic ulcer, especially in the area of Glasgow, and particularly in men there were more duodenal than gastric ulcers. The incidence of gastric ulcer in women has long been noted to be much greater than that in men and to occur at an early age while the incidence of duodenal ulcer although less common has long been recognized as more frequent in men. The examination by means of x rays, the chemical analysis of the gastric contents, and the testing of the feces for blood are methods of examination that have for many years been giving increasing accuracy to the diagnosis of these cases. Since these methods have been perfected during and after the first Great War the hospital statistics of the last twenty years are far more important than those of earlier periods.

By means of a series of charts the author covers the hospital returns for admissions of peptic ulcer at the Western Infirmary of Glasgow for the period from 1897 to 1942, inclusive. Chart I gives the returns for gastric ulcer duodenal ulcer and hematemesis in men. It shows a marked increase in the frequency of ulceration, especially of duodenal ulcer in the last twenty years and remarkably low figures in the earlier years. By contrast, Chart II gives similar returns for women showing high figures for gastric ulcer mostly in younger women in the years from 1897 to 1907 with a gradual decrease from then on. This is no doubt related to the prevalence of chlorosis in those earlier years. In both these charts the relative frequency of gastric and duodenal ulcers may be considered to be more accurate in the later years. Even today in medical cases, in spite of modern methods, it is sometimes difficult to be sure whether the ulcer is gastric or duodenal. Forty years ago the possibility of a duodenal origin was just beginning to be appreciated. It is possible too that in the earlier years, cases diagnosed as gastritis or gastric catarrh were in reality cases of peptic ulcer. This may further explain the contrast between the later and the earlier years.

One might suspect that a larger number of patients being admitted to the hospital might explain the large figures of recent years, but the admissions to medical wards over the period only increased from about 1,500 in 1897 to about 2,300 in 1942 while the increase of admissions to surgical wards was much greater from about 4,500 to 11,500. Chart III shows the numbers for peptic ulcer (gastric, duodenal, and hematemesis) in medical wards for

men and women, a composite picture of Charts I and II. It shows again the preponderance of peptic ulcer in the early years and its comparative infrequency for the period from 1908 to 1924. The later extraordinary increase of duodenal ulcer is graphically shown. This chart corresponds with remarkable accuracy with Chart IV which gives the record of abdominal sections for perforated ulcer many of these cases undoubtedly having been in medical wards previously.

The first recorded abdominal section for perforation was done in 1897 it was a gastric perforation. The first operation for a perforated duodenal ulcer was done in 1900. Without doubt many perforations occurred and went untreated in those earlier years much as happened previously with appendicitis. The medical profession learned to diagnose perforation and the remarkable success of the surgeons in dealing with those cases led to their being sent to the hospital as soon as possible. We may therefore safely assume that the majority of these perforations have been surgically treated for the past twenty years.

Chart IV shows a tremendous and steady rise of perforations (gastric and duodenal) operated on from 31 in 1921 to the great total of 206 in 1941. The increase was accounted for mainly by the increase in duodenal cases occurring mostly in men. Although some hemorrhage and perforation some times occur in patients with no previous history there usually is a definite history of months or years sometimes of from twenty to thirty years or more, and the same chronic case may develop both of these serious complications. The experience of Alacrae an expert in abdominal surgery was that in his wards (Western Infirmary) 75 per cent of cases of duodenal perforations had a history of over three years symptoms and that 10 per cent had a history of over ten years symptoms. In the light of findings such as these the appearance of perforation or hemorrhage can scarcely be linked to some recent cause.

While this interesting study does little more than call attention to the prevalence of peptic ulcer and its rather appalling increase in recent years it invites considerable speculation as to the primary cause. No solution is as yet forthcoming. The close relationship between the ulcer and the presence of gastric juice has incriminated hydrochloric acid as a causal factor. The typical peptic ulcer is met with only at the lower end of the esophagus, in the stomach, in the first part of the duodenum and more recently in the jejunum at or near the stoma following gastrojejunostomy. The hydrochloric acid of gastric juice in at least the earlier stages of peptic ulcer is found to be higher than normal and this favors that assumption. The author is inclined to think that the primary condition is an erosion of the mucous membrane which is acted upon by the gastric juice, and this stimulates an excess of gastric juice, which causes, in fact, somewhat of a vicious circle. The problem to be solved would seem to be what causes these erosions?

General health, anemia, overfatigue and mental anxiety would be of resistance while heredity is a definite susceptibility. However, these factors do not explain the primary cause. In the case of a diet factor does not seem to provide an explanation. The author states "since the beginning of this century there has been wars, industrial stress and the strain of unemployment, and recently there has been the bombing of so many of our cities and these may have had an influence. But the contrast of the incidence of ulcers in men with that in women during recent years can hardly be explained by such causes as it would seem women have been exposed to these conditions as much as men. The author adds that the high incidence of perforation and the quite serious mortality from septicemia rather seem to be a reflection on the local treatment and would seem to indicate more after care. It is to be hoped that investigations which have been carried out by S. Wolf and H. S. Wolf (New York 1912) may help to solve the difficulties of determining some primary cause of this rather serious disease. Morris J. Saiter, M.D.

Walt on Sir J. Marsh H. C. J. Evans H. H. Tidy Sir H., and Others: Discussion on Treatment of Duodenal Ulcer. *Proc. R. Soc. Med. Lond.* 1934, 27, 3.

This report gives the views of several known members of the Royal Society of Medicine on the treatment of duodenal ulcer. Sometimes there is conflict but the crux of the discussion with regard to surgical treatment of the duodenal ulcer revolves about the choice of procedure between gastroenterostomy and gastrectomy. It is brought out that a type of surgical treatment that is effective in a kind of surgeon's hands may be ineffective in the hands of another. Moreover the social environment of each patient has a direct bearing on the case. Likewise the habitat of a locale produces differences in the character of the ulcer.

Dr. JAMES WALTON, president of the Section of Surgery, opened the discussion by warning the younger surgeons not to accept the written word without question but to find the truth for themselves. He said that this danger Walton is warning them against very strongly to be aware of and avoid. He said that in the determination of which he can conscientiously find his results to give the method of treatment. He said that immediately after the last World War, the results of the treatment were equal with what he said that he had found to be the best course of treatment. He said that Walton's views are based on the fact that he is a surgeon of study. He said that he had never said that "no man is fit to say that form of treatment is a cure cure. And that he said that he had found the best results in his own hands. There are a lot of different things that

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The discussion as to operative technique in England for uncomplicated cases is principally between gastroenterostomy and partial gastrectomy. In a few cases local excision with plastic procedure of the pylorus may be the method adopted. The balance between posterior gastroenterostomy and partial gastrectomy depends upon the frequency of gastric junctional ulceration after posterior gastroenterostomy. Walton calls attention to the many reports that have been published by continental surgeons and some from the United States showing an incidence of from 1 to 15 per cent. These reports, he believes, have undoubtedly influenced many English surgeons, but he said that with conditions quite dissimilar to those in the countries whence the reports are issued and where partial gastrectomy seems to be the rule.

Walton said that in his carefully chosen follow-up series the incidence has always been about 5 per cent and that these results have been constant. Moreover he said that while partial gastrectomy reduces the acidity to a greater degree it does not entirely remove the danger of this complication. In his series of 16 gastric junctional ulcers a partial gastrectomy had been previously performed in 12. There can be little doubt that of the two procedures partial gastrectomy is the more severe. While many series have been published with a very low mortality it must be remembered that the operations were performed by surgeons exceptionally skilled in this technique. In the hands of the general practitioner this technique would probably show a death rate of between 5 and 10 per cent, whereas with gastroenterostomy it should not be more than 1 per cent. Walton's conclusion is that in duodenal ulcer by posterior gastroenterostomy whether or not they be gastric stenosis and to serve partial gastrectomy for 10 per cent of cases that have ulcerated gastric junctional ulcer. Nevertheless, he would not feel able to determine the case which are likely to develop gastric junctional ulcer and to perform a gastric resection on them. He said that he knew he could control the acidity in the stomach but that they are probably cases in which the ulcer has been already healed and cases in which the ulcer is actually healing.

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General ill health, anemia, overfatigue, and mental anxiety would lower resistance, while heredity might determine a susceptibility. However, these factors do not explain the primary cause. Diet, alcohol and tobacco do not seem to provide an explanation. The author states: Since the beginning of this century there have been wars, industrial stress and the strain of unemployment, and recently the added distress resulting from the bombing of so many of our cities, and these may have had an influence. But the contrast of the incidence of ulcers in men with that in women during recent years can hardly be explained by such causes as it would seem women have been exposed to these conditions as much as men. The author adds that the high incidence of perforation and the quite serious mortality from severe hemorrhage seem to be a reflection on medical treatment and would seem to indicate more after-care. It is to be hoped that investigations on the lines of those carried out by S. Wolf and H. S. Wolf (New York 1932) may help to solve the difficulties of determining some primary cause of this really serious disease. *M. THOMAS J. SALTER, M.D.*

Walton, Sir J., Marshall, C. J., Evans, H. Tidy, Sir IL and Others: Discussion on Treatment of Duodenal Ulcer. *Proc R Soc Med Lond* 1934 38 9

This report gives the views of several well known members of the Royal Society of Medicine on the treatment of duodenal ulcer. Sometimes these views conflict, but the crux of the discussion with regard to surgical treatment for duodenal ulcer revolves about the choice of procedure between gastroenterostomy and gastrectomy. It is brought out that a type of surgical treatment that is effective in a skilled surgeon's hands may be ineffective in the hands of another. Moreover the social environment of each patient has a direct bearing on the case. Likewise habitat or locale produces differences in the character of the ulcer.

Sir JAMES WALTON, president of the Section of Surgery, opened the discussion by warning the younger surgeons not to accept the written word without question but to find the truth for themselves. To counteract this danger Walton considered it essential for every surgeon to have a well organized follow up department in which he can conscientiously study his own results to prove his methods, if indicated. Immediately after the last World War Walton's hospital in London was equipped with what appears to be the first clinic of this sort in Great Britain. Walton's views are based on this twenty-five year follow up study. Since technical surgery is an art, he states, "no man is entitled to say that one form of treatment is alone correct. All that he can say is that it gives the best results in his own hands, others may find different methods more suitable."

It is generally conceded that the one indication for surgical interference is the failure of medical treatment. The presence of stenosis or hemorrhage

or even of perforation is in a sense evidence of this failure. Walton asserts that the standard of cure varies with the social position of the individual patient. Thus, a man in comfortable circumstances may keep free of symptoms and be apparently cured on a diet and in a sheltered life, whereas the demands made upon a working man entail an entirely different set of conditions which would prove inadequate for such an instance.

The decision as to operative technique in England for uncomplicated cases lies principally between gastric resection and partial gastrectomy. In a few cases local excision with plastic procedures upon the pylorus may be the method adopted. The choice between posterior gastroenterostomy and partial gastrectomy depends upon the frequency of gastrojejunal ulceration after posterior gastroenterostomy. Walton calls attention to the many reports that have been published by continental surgeons and some from the United States showing an incidence of from 3 to 35 per cent. These reports, he believes, have unduly influenced many English surgeons, who have to deal with conditions quite dissimilar to those in the continent, hence the reports are misused and where partial gastrectomy seems to be the rule.

Walton states that in his carefully controlled follow up result the incidence has always been about 4 per cent, although these results have been constant. Moreover he states that while partial gastrectomy reduces the acidity to a great degree it does not entirely remove the danger of this complication. In his own series of 176 gastrojejunal ulcers a partial gastrectomy had been previously performed in 12. There can be little doubt that of the two operations partial gastrectomy is the more severe. While many series have been published with a very low mortality it must be remembered that the operations were performed by surgeons exceptionally skilled in this technique. In the hands of the general practitioner this technique would probably show a death rate varying between 5 and 10 per cent, whereas with gastroenterostomy it should not be more than 1 per cent. Walton's custom is to treat duodenal ulcers by posterior gastroenterostomy, whether or not they be causing tenosis and to reserve partial gastrectomy for the 4 per cent of cases that have developed a gastrojejunal ulcer. Nevertheless, he considers it feasible to determine the cases which are likely to develop gastrojejunal ulcer and to perform a primary gastrectomy on them. Increasing knowledge has contributed greatly to distinguishing these cases. As a rule they are probably cases in which the ulcer has begun early in life and cases showing an unusually high acidity.

HARMON TAYLOR, Walton's coworker, has also noted that the presence of hyperplastic gastritis as revealed by the gastroscope is a danger signal in such cases. In these cases Walton performs a partial gastrectomy. At the present time his preference is in the form of gastrectomy lies in the end-to-end gastroduodenostomy known as the Billroth I operation as it more closely follows the normal anastomosis and in his

experience seems to cause less operative disturbance but if the ulceration is extensive or the duodenum widely stenosed the Polya method is selected and gives good results. Walton believes that the modern tendency to divide the duodenum beyond the ulcer is unnecessary and adds to the risk. If the duodenal stump is securely closed, any area of active ulceration that may be left in the blind stump will always heal.

The surgical treatment of perforation may require more than simple suture to effect a permanent cure. Perforated ulcers are chronic lesions and recurrences sometimes take place. Walton states that in his own practice alone 63 cases were found which required an operation for an ulcer recurring or persisting after a previous simple suture for perforation. In England the accepted teaching is to do no more than a simple suture for perforation. In Russia and the Scandinavian countries the tendency is toward more radical steps, many of the cases being treated by immediate gastrectomy. Walton states that if one or two mattress sutures are used a firm closure can nearly always be brought about and reinforcement with omentum is unnecessary. He believes that there is a dangerous dogmatism today in denying the use of drainage. A suprapubic drain can never do any harm and while many cases do well without it Walton asserts that he has seen a number of examples of pelvic and subphrenic abscess which might have been prevented had drainage been instituted. A case of perforation that has recovered with simple suture must be carefully watched in a follow up department and not sent away as cured. There are so many recurrences that, in spite of all statements to the contrary Walton is convinced that a surgeon with wide experience is justified in early cases, in performing a gastroenterostomy at the first operation. His own figures have shown that the mortality is not increased thereby if a wise discrimination is made.

In the treatment of hemorrhage each surgeon must formulate his treatment upon the results of his own experience. The published mortality of cases treated medically varies from 4 to over 50 per cent. Walton treats all cases whether due to acute or chronic ulceration medically and operates only if both the physician and he himself believe that a second hemorrhage is probable and that if it occurs it will be fatal. Or if the hemorrhage has already recurred and the patient has survived a blood transfusion must always be given if an operation is undertaken being commenced immediately before the operation is started and continued as a drip transfusion after the operation. In theory undoubtedly the most satisfactory method of control would be the performance of a partial gastrectomy but the majority of surgeons believe that such an operation would generally be too severe a strain upon so ill and enfeebled a patient. The method of ligating arteries running to the ulcer which is often advocated has in Walton's experience generally been a failure for the arterial anastomosis is so free. Often the ulcers are

so large that any form of local excision is impracticable. In many cases of duodenal ulcer the anterior wall of the duodenum may be so widely invaginated by a running mattress suture that the lumen is entirely occluded and the anterior wall pressing firmly upon the ulcer safely controls the hemorrhage. The operation is completed by the performance of a posterior gastroenterostomy. In other patients, however the duodenal wall is so indurated that invagination is impossible. Under these conditions and with all large gastric ulcers the safest and most satisfactory method consists of opening the viscus underpinning the bleeding vessels and suturing the ulcer crater with interrupted mattress sutures. In the case of the duodenum the opening in the anterior wall should be embedded after suture and a posterior gastroenterostomy performed.

C. JENNINGS MARSHALL, the next speaker asserted that the primary treatment of duodenal ulcer is medical, the essential of which is physical and mental rest the one common factor of varied successful regimes and that in the treatment of severe bleeding symptoms disappear as rapidly with waterfasting as with any drug and diet system. It is vital however to distinguish between cure of the symptoms and cure of the ulcer as the ulcer persists long after disappearance of the x ray signs and occult blood in the feces. The hydrochloric figure by no means represents the peptic activity and is unreliable for estimation of progress and prognosis. While certain food abstentions relieve or minimize symptoms they cannot be relied on to secure freedom from recurrence nevertheless, only about one sixth of the cases need surgical intervention.

Perforation rarely heals without surgery and recurrent perforation calls for radical measures as does recurrent bleeding. Individual massive hemorrhages are primarily to be treated by functional rest and by leaving the blood pressure at the lowest level warrantable. Only after four or five days, when it is clear that arrest is not obtained, must surgery be considered. Massive transfusion then makes it possible to deal with a very difficult technical problem. Progressively frequent and more severe relapses leading to invalidism constitute the remaining surgical indication.

Undoubtedly a proportion, less than half of gastroenterostomies are very satisfactory. Gastrectomy is becoming less and less dangerous with adequate preparation oral hygiene, lavage, and attention to the hemoglobin and blood colloids breathing exercises and muscular and vascular tonus. Subjects with a good Bloots-McKesson ratio are suitable for spinal analgesia. bad risks need local and splanchnic blocking with cyclopropane or gas and oxygen. Prolonged anoxemia leads to serious postoperative myocardial danger. The stomach should be resected from high on the lesser curve to a little below the spleen. In deeply penetrating and extensive duodenal ulcer the stomach may be divided $\frac{1}{3}$ in proximal to the pylorus but it is essential to enucleate the antral mucosa. The possibility of leakage

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Perforation rarely heals without surgery and recurrent perforation calls for radical measures as does recurrent bleeding. Individual massive hemorrhages are primarily to be treated by functional rest and by leaving the blood pressure at the lowest level warrantable. Only after four or five days when it is clear that arrest is not obtained must surgery be considered. Massive transfusion then makes it possible to deal with a very difficult technical problem. Progressively frequent and more severe relapses leading to invalidism constitute the remaining surgical indication.

Undoubtedly a proportion, less than half of gastroenterostomies are very satisfactory. Gastrectomy is becoming less and less dangerous with adequate preparation oral hygiene, lavage, and attention to the hemoglobin and blood colloids, breathing exercises, and muscular and vascular tonus. Subjects with a good Moots-McCleson ratio are suitable for spinal analgesia. bad risks need local and splanchnic blocking with cyclopropane or gas and oxygen. Prolonged anoxemia leads to serious postoperative myocardial danger. The stomach should be resected from high on the lesser curve to a little below the spleen. In deeply penetrating and extensive duodenal ulcer the stomach may be divided $\frac{1}{4}$ in proximal to the pylorus but it is essential to enucleate the antral mucosa. The possibility of leakage

calls for precautionary drainage down to any dubious stump. Gastroduodenal anastomosis is permissible only when there is no gross stenosis or infection. The Polya Moynihan operation is frequently followed by "dumping" into the jejunum and duodenal reflux. The opening should be a little larger than gut caliber and the proximal jejunum should be hitched up to the gastric suture line an inch or so above the union.

HORACE EVANS approaches the subject of treatment of duodenal ulcer more generally from the medical angle. He asserts that while the diagnosis of duodenal ulcer is relatively easy in most patients and confirmation by means of x-ray satisfactory the history may in some instances be quite atypical, and conversely a typical history may be quite deceptive. This is true particularly he states, when the condition occurs in women. The frequency with which complications such as hemorrhages, perforation, and even stenosis occur in patients who have minimal symptoms of indigestion is surprising, although, no doubt, this is due in some of them to the fact that the ulcer is of a more acute type. This type of ulcer or superficial erosion may heal with little residual deformity and so reveal no x-ray change very soon after a hemorrhage.

Evans believes the treatment of duodenal ulcer to date remains eminently unsatisfactory. He considers the most satisfactory basic treatment to be essentially "medical," surgery being a useful aid in selected cases. He admits that surgery is essential in certain instances, as for example in perforation, pyloric obstruction, chronic perforating or adherent ulcers, and possibly in certain rare examples of hemorrhage in older patients. Likewise there are patients in whom adequate medical treatment has failed. In these cases gastroenterostomy and partial gastrectomy perhaps to an even greater extent, may yield excellent results. It is true, however that at medical clinics patients with postoperative ulcer who appear to have escaped surgical statistical surveys, lurk about in no small numbers.

Evans states that in the past five years he has been impressed by certain aspects of medical treatment. For instance he has found satisfactory healing to be unusual if the patient is ambulant. Complete bed rest for a minimal period of six weeks, followed by a further six weeks of quiet convalescence, is essential. In this disease the early disappearance of the pain, together with a host of economic and domestic difficulties, is an important factor in the generally unsatisfactory results. Mental relaxation is undoubtedly as important as physical. Evans regards phenobarbitone as of more importance than alkalis in this condition, the latter being demanded only when treatment is inadequate. He asserts that the frequency of food is probably of more importance than the nature of the food. In hospital practice the results of treating these patients in a special ward are striking. The necessary regime is universal and more easily and satisfactorily carried out. "the total exclusion of unsuitable foods, tobacco and

perhaps even the surgeon, makes the burden easier and recovery more rapid." The good psychological reaction under such conditions is worthy of note.

Evans states that in view of the unsatisfactory state of our present knowledge each patient must be managed according to his condition. Consideration should be given not only to the ulcer but to each patient's individual characteristics, economic factors, occupation and so on, all demanding particular attention. He believes that in all but the clearest cases it is good practice to co-operate with a surgeon from the outset, whether surgery is immediately in question or not. If the need for surgery arises, the importance of the state of the lungs, the presence of anemia, and possible dietetic deficiencies cannot be overemphasized. The risk of chest complications, so common after gastric operations, should be minimized by preoperative instruction in breathing exercises and the avoidance of the too tight abdominal binder rather than by the choice of anesthetic.

Sir HENRY TUDY, the next speaker called attention to the differences in the character of peptic ulcers observed in England and on the Continent, as well as to the differences between those seen in London and England and Scotland. He states that in London gastric ulcer is considerably more common than duodenal ulcer at the present time, while in Scotland duodenal ulcer is much more prevalent than gastric ulcer. Differences in the incidence of the two types of ulcer exist also in various social classes.

Tidy is of the opinion that our views on gastric pathology need revision, especially in view of the work of Wolf and Wolff (New York, 1943) who found that they could produce chronic gastric ulcer in four days and heal it in five days. The position is the same for gastritis. Gastroscopists now recognize the rapidity with which the gastric mucous membrane can change.

Tidy stresses the importance of discussion from time to time of the relative merits of medical and surgical treatment for peptic ulcers, since both are changing. Surgeons often appear to be satisfied that medical treatment has failed when the treatment followed would not have satisfied a physician. Frequently when a first course of medical treatment fails, a second course is successful.

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years ago von Eiselsberg showed how frequently a gastrojejunal ulcer developed if the pylorus were left. Pannett declared he had given up the Billroth I anastomosis because the results following it were not so good as those following an operation of the anterior Polya type. He attributed this to the diminished mobility of the stomach which the former operation imposed.

The last speaker Taylor declared that he was not so much concerned with the treatment of acute complications, as with the situation which developed when a patient found himself having worse and worse pain and losing more and more time at his work in spite of all he could do in the way of conservative treatment. This type of patient calls for operative treatment, but the problem arises which operation to perform—partial gastrectomy or a gastroenterostomy. The former is without any question the more extensive and dangerous operation, but many surgeons have come to adopt it as a routine because of the incidence, about 25 per cent of anastomotic ulceration after gastroenterostomy. It is true that when gastroenterostomy is used indiscriminately the results are quite unpredictable; the operation in some cases being followed by complete and permanent relief of symptoms, but in others serving merely to aggravate them. What is needed is a means of preoperative segregation of the minority of potential failures of gastroenterostomy—partial gastrectomy being reserved for these, while gastroenterostomy is to be done in the majority of the cases. The speaker considered the test meal of some help, but too unreliable for this purpose. Taylor had employed a gastroscopic method with some success; he presented this method at the meeting. Eight years previous he had undertaken a gastroscopic study of the cases with persisting symptoms after gastroenterostomy in Sir James Walton's Follow Up Department at the London Hospital. The outstanding observation was that all these patients had a marked excess of gastric folds. Six control cases which had been cured by gastroenterostomy showed nothing like this degree of rugosity although the number of folds was more than in the average stomach.

These findings appeared to embody an explanation of the failure of gastroenterostomy in some cases and its success in others. It seemed that this operation would not be followed by stomal ulceration unless the gastric mucosa was grossly redundant, probably because of habitual hyperacidity. For the last six years Taylor has therefore gastroscopied all cases of duodenal ulcer before operation, and performed a partial gastrectomy on those with marked rugosity and a gastroenterostomy on the others. It was suggestive that the proportion of partial gastrectomies amounted to 25 per cent, just about the number of failures that would have been anticipated if all the cases had been subjected to gastroenterostomy.

The speaker considered it too early to draw final conclusions from these results, but he believed that they justified a return to the operation of gastroenterostomy except in those cases in which a gas-

troscopic estimation of the degree of rugosity in the stomach indicated the danger of recurrent ulceration. Only then was the more hazardous operation of partial gastrectomy justified.

MATTHIAS J. SKIFFERT, M.D.

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The earliest experiences with the surgical treatment of ileitis seemed eminently satisfactory.

Experience in 164 instances of enteritis, terminal ileitis, and combined ileocolitis operations performed by many surgeons in many institutions is reported.

A primary resection of the disease process, usually of the pathological terminal ileum and the adjacent normal ileum and ascending colon was performed in 55 cases. Nine patients died postoperatively. Of the remaining 46, 9 developed recurrences in the ileum above the point of anastomosis, a recurrence rate of 19.5 per cent.

An ileotransverse colostomy or ileosigmoidostomy with transection of the ileum was carried out in 65 cases with no operative death but 9 recurrences of the disease must be recognized, a recurrence rate of 13.8 per cent.

A two-stage ileocolic resection which consisted of a primary short-circuiting ileocolostomy above the lesion with transection of the ileum followed after a period of time by resection of the original area of disease in the terminal ileum, cecum and ascending colon was done on 25 patients, with 3 postoperative deaths a mortality of 12 per cent. Eight instances of recurrent disease in the surviving 22 patients, a rate of 36.3 per cent, were noted.

No satisfactory medical treatment of ileitis exists. Chemotherapy has not been proved to be generally satisfactory in this disease.

Until the cause of the disease is discovered the treatment of ileitis remains surgical. The future improvement in the results of the operative treatment will rest on earlier diagnosis and more prompt operative intervention. With earlier diagnosis on the part of the physician and with greater experience on the part of the surgeon, especially as regards the choice of operative procedure, the future should hold promise of far better results.

HARRY W. FINEK, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Dixon, C. F. and Lichtman, A. L. Congenital Absence of the Gall Bladder. *Surgery* 1945 17 11

This article is based on 50 cases of congenital absence of the gall bladder that have been reported since 1900 and on 10 cases that have been observed at the Mayo Clinic. Symptoms resembling those of cholelithic disease were present in 58 per cent of the 60 cases. Forty-eight per cent of the patients had jaundice and 27 per cent had stones in the common bile duct. Symptoms were present in 73 per cent of

calls for precautionary drainage down to any dubious stump. Gastroduodenal anastomosis is permissible only when there is no gross stenosis or infection. The Polya Moynihan operation is frequently followed by "dumping" into the jejunum and duodenal reflux. The opening should be a little larger than gut caliber and the proximal jejunum should be hitched up to the gastric suture line an inch or so above the union.

HORACE EVANS approaches the subject of treatment of duodenal ulcer more generally from the medical angle. He asserts that while the diagnosis of duodenal ulcer is relatively easy in most patients and confirmation by means of x-ray satisfactory the history may in some instances be quite atypical, and, conversely a typical history may be quite deceptive. This is true particularly, he states, when the condition occurs in women. The frequency with which complications such as hemorrhages, perforation, and even stenosis occur in patients who have minimal symptoms of indigestion is surprising, although, no doubt, this is due in some of them to the fact that the ulcer is of a more acute type. This type of ulcer or superficial erosion may heal with little residual deformity and so reveal no x-ray change very soon after a hemorrhage.

Evans believes the treatment of duodenal ulcer to date remains eminently unsatisfactory. He considers the most satisfactory basic treatment to be essentially medical, surgery being a useful aid in selected cases. He admits that surgery is essential in certain instances, as for example in perforation, pyloric obstruction, chronic perforating or adherent ulcers, and possibly in certain rare examples of hemorrhage in older patients. Likewise there are patients in whom adequate medical treatment has failed. In these cases gastroenterostomy and partial gastrectomy perhaps to an even greater extent, may yield excellent results. It is true, however, that at medical clinics patients with postoperative ulcer who appear to have escaped surgical statistical surveys, lurk about in no small numbers.

Evans states that in the past five years he has been impressed by certain aspects of medical treatment. For instance he has found satisfactory healing to be unusual if the patient is ambulant. Complete bed rest for a minimal period of six weeks, followed by a further six weeks of quiet convalescence, is essential. In this disease the early disappearance of the pain, together with a host of economic and domestic difficulties, is an important factor in the generally unsatisfactory results. Mental relaxation is undoubtedly as important as physical. Evans regards phenobarbitone as of more importance than alkalis in this condition, the latter being demanded only when treatment is inadequate. He asserts that the frequency of food is probably of more importance than the nature of the food. In hospital practice the results of treating these patients in a special ward are striking. The necessary regime is universal and more easily and satisfactorily carried out "the total exclusion of unsuitable foods, tobacco, and

perhaps even the surgeon, makes the burden easier and recovery more rapid." The good psychological reaction under such conditions is worthy of note.

Evans states that in view of the unsatisfactory state of our present knowledge each patient must be managed according to his condition. Consideration should be given not only to the ulcer but to each patient's individual characteristics, economic factors, occupation and so on, all demanding particular attention. He believes that in all but the clearest cases it is good practice to co-operate with a surgeon from the outset, whether surgery is immediately in question or not. If the need for surgery arises, the importance of the state of the lungs, the presence of anemia, and possible dietetic deficiencies cannot be overemphasized. The risk of chest complications, so common after gastric operations, should be minimized by preoperative instruction in breathing exercises and the avoidance of the too tight abdominal binder rather than by the choice of anesthetic.

Sir HENRY TIDY, the next speaker called attention to the differences in the character of peptic ulcers observed in England and on the Continent, as well as to the differences between those seen in London and England and Scotland. He states that in London gastric ulcer is considerably more common than duodenal ulcer at the present time, while in Scotland duodenal ulcer is much more prevalent than gastric ulcer. Differences in the incidence of the two types of ulcer exist also in various social classes.

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the cases in which the patients were more than forty five years of age. Prolonged drainage of the common bile duct with a T tube is advocated in the cases in which symptoms are present.

Keynes, G: Rupture of the Pancreas. *Brit. J. Surg.* 1944, 3 300.

Two cases of rupture of the pancreas and its duct in young soldiers are presented. Both cases were uncomplicated at first, but one patient developed a persistent fistula, and both had serious complications during the postoperative course. Both of the patients recovered. The second case is of particular interest because it is probable that the rupture of the pancreas was due to under water blast, apparently the only example of this injury that has been described.

The first patient, aged twenty, was injured while riding a bicycle and colliding with a boom placed across a runway. He was struck in the epigastrium and shortly thereafter developed signs of acute abdominal crisis. Immediate operation revealed a rupture of the body of the pancreas over the vertebral column. No other viscus was injured. Drainage to the region of the injury was established. The fistula healed spontaneously but three months later it was found that a large pseudocyst had formed. This lesion was opened and drainage was re-established.

Roentgenographic study after lipiodol injection of the fistula indicated that the duct of Wirsung had been ruptured, since lipiodol entered the left two-thirds of the duct, but could not be seen to enter the right one third. Since spontaneous permanent healing of the fistula would not be likely without patency of the duct, it was decided to implant the fistula into the jejunum. This was done according to the procedure of Lehey and Llum. For several months after operation the patient experienced attacks of

abdominal disturbance, but he has been quite well for the past six months.

The second patient, aged twenty two was in a flying boat which crashed into the sea. He stated that he was uninjured in the crash and felt perfectly normal, having floated upright in the water supported by a Mae West belt. He was about 400 yards from a U boat which exploded as it sank from a depth bomb that had been dropped in its conning tower. At the moment of explosion he felt a peculiar sensation in the abdomen which he described as a "rumbling in the belly." He was rescued treated for shock, and operated upon about nineteen hours later. Operation revealed free blood in the peritoneal cavity and a tear in the peritoneum on the outer side of the hepatic flexure of the colon with retroperitoneal hemorrhage in this area. The retroperitoneal space was drained through a stab wound in the loin, the colon was sutured back in place, and the abdomen was closed. On the tenth day he developed a large swelling in the epigastrium, which was regarded as a pseudocyst of the pancreas, and the following day developed signs of acute intestinal obstruction. A second laparotomy was performed and the lesser peritoneal sac was opened through the gastrosplenic ligament. About 3 pints of muddy fluid were evacuated and examination of the pancreas through the opening revealed a vertical tear through the middle of the body. Ten days later he again developed signs of acute intestinal obstruction and a third laparotomy was performed. This revealed a volvulus of a loop of small intestine, which was reduced and the abdomen was closed. Drainage from the lesser peritoneal sac ceased about seventeen days after the second laparotomy. The patient had to undergo a fourth operation for repair of the large ventral incisional hernia. There were no further complications and he returned to full duty two months later.

JOHN L. LUNDQUIST M.D.

GYNECOLOGY

UTERUS

Hafer J F: Conization and Early Diagnosis of Carcinoma of the Cervix. *Am J Surg* 1945 67 68

Carcinoma of the cervix is a common malignant lesion in the female. Its early diagnosis is absolutely essential for its successful treatment. The most certain way of making this diagnosis is by biopsy.

The author routinely does a radical conization of the cervix before subtotal hysterectomy for two reasons, (1) to sterilize the cervix, and (2) to obtain a biopsy. He has had no serious complications as a result of the conization. If the lesion on the cervix was suspected of malignancy, he always did a radical conization believing that if the cervix was not malignant, the removal of diseased tissue might have some prophylactic effect.

The conization is bloodless because of careful adjustment of the cutting and coagulation currents. A high current is used to achieve fast cutting with only a very thin layer of coagulation.

All patients for conization are admitted to the hospital. The most suitable time for conization is immediately after the menstrual period. When radical conization is done the patient receives sodium pentothal and oxygen and is hospitalized for three days postoperatively.

The patient is placed in the lithotomy position, the cervix and vagina are cleansed and the conization is carried out, the size of the loop being varied according to the size of the cervix and the amount of tissue that is to be removed. Before leaving the hospital the patient is instructed to avoid intercourse for four weeks, to take daily hot sitz baths, and not to be alarmed if menstrual bleeding occurs. On the fourth or fifth day the thin necrotic layer of tissue will slough and expose the granulation tissue underneath. This will have a slight tendency to bleed.

Only 2 patients in the entire series had to be hospitalized for bleeding. This occurred within one to two weeks after conization. The slough completely disappears in from three to six weeks and the cervix is smooth and has the appearance of almost a nulliparous cervix. Little or no scar tissue results from proper conization. Only moderate stricture formation was observed in 2 patients in the check up following radical conization.

Conization was done in 311 cases between July 1942 and October 1944. Among these 311 patients 18 malignancies and 11 squamous-cell metaplasias were found. All patients with metaplasia were urged to return for repeated check ups but comparatively few did so. Four cervical carcinomas were found accidentally in this series.

The author advocates conization for the prevention as well as for the diagnosis of malignancy of the cervix.

HENRY C. FALK, M.D.

Scheffey L. C. Farrell, D. M. and Hahn, G. A.: The Role of Injudicious Endocrine Therapy in the Delayed Diagnosis of Uterine Cancer. *J Am Med Ass* 1945 127 76.

The authors call attention to a practice that is proving to be a serious factor in the delayed diagnosis of uterine cancer namely the indiscriminate use of endocrine therapy for the control of abnormal bleeding from the genital tract, when an organic cause for such hemorrhage has been either undiscovered or ignored. Delay in diagnosis is the most important explanation of the low curability rate of uterine cancer.

Granted that cancer of the uterus may exist in a very small minority of patients without causing any untoward symptoms whatever clinical experience and statistics prove that in the vast majority of instances abnormal bleeding from the genital tract is the most frequent symptom of the disease.

Cervical cancer may occur at any time during the reproductive period although the majority of patients afflicted are in the menopausal or postmenopausal period. Twenty-seven per cent of the patients observed in the Department of Gynecology of the Jefferson Medical College Hospital, Philadelphia, have been women under forty years of age when first seen.

Biopsy must be depended on for certainty of diagnosis. Fundal cancer is usually manifested primarily by postmenopausal bleeding. This has been true in 79 per cent of such patients seen at this hospital. The remaining 21 per cent were over forty years of age however and had not yet ceased menstruating when the diagnosis was made.

Curettage is essential to establish an accurate diagnosis and to determine proper treatment.

When abnormal bleeding is present during the late reproductive, menopausal, or postmenopausal periods there is much less justification for prolonged and experimental endocrine therapy. Well recognized radiological and surgical measures are available in such cases, not only for the relief of organic pelvic disease, but even for the correction of proved functional bleeding—measures that are surer and far less time-consuming than prolonged and often ineffective endocrine therapy.

HARRY W. FRANK, M.D.

EXTERNAL GENITALIA

Compton B. C. Bieren, R. E., Jones, E. G. Inoles B. II., Jr and Others: The Treatment of Gonococcal Vulvovaginitis. *J Am. Med Ass* 1945 127 6.

The authors studied 442 cases of vaginal discharges in children 318 (72 per cent) showed gonococci on direct smear.

In this study a careful history was taken and included duration of the illness, the number of chil-

dren in the home, the individuals with whom the child slept and played and the school which the child attended.

A complete physical examination was made, including examination of the breasts for tenderness, secretion, and size. The amount of vaginal discharge or bleeding was noted. A smear was taken by inserting an applicator high in the vagina on each visit.

On making the diagnosis the mother was told the importance of relative isolation of the child and instructed in the use of the commode, towels, and clothing.

The child was examined at weekly intervals until three successive smears were negative. She was then seen at monthly intervals until the smears had been negative for three months. She was then seen at three-month intervals, and discharged when well for one year.

The child was allowed to return to school as soon as the symptoms entirely cleared and the smear became negative.

Of the 318 cases of gonococcal vulvovaginitis which were diagnosed and treated, 153 were successfully followed up for one year after the smear became negative. Of the 153 cases, 122 were treated with oral or vaginal-suppository estrogens (natural or synthetic), 12 with sulfathiazole or sulfadiazine, 10 with a combination of estrogens and sulfonamide drugs, 6 with Floraqin suppositories or insufflation, and 1 with Floraqin and estrogen.

Of the 122 patients treated with estrogens, 33 had a recurrence. Of the 12 treated with sulfonamide drugs, 2 had a recurrence.

In the sulfonamide cases the discharge diminished in two or three days. The smears became negative by the end of the second week. No patient was treated with a sulfonamide drug longer than three weeks. No untoward reactions were noted. The dosage of sulfathiazole which was given orally was 0.5 gm. per day to children from six months to one year, 1 gm. per day to children from one year to four years, and from 1.5 to 2 gm. per day to children between five and ten years. Sulfadiazine was given orally in half the dose for sulfathiazole.

The estrogens were used either as suppositories (natural or synthetic) or in oral medication (synthetic). The dosage of diethylstilbestrol was 0.5 mgm. per day for children between six months and one year, and from 1 to 3 mgm. per day between one year and ten years.

The average total dose of natural estrogens until complete cornification and a negative smear occurred was approximately 35,000 international units.

The most common untoward reaction was an effect on the secondary sex characteristics, slight hypertrophy of the breasts, clitoris, and labia. A few children developed nausea, slight vaginal bleeding, or the growth of pubic hair. All of these changes

receded as soon as the drug was stopped; no permanent change was noted.

In the estrogen treated cases the discharge disappeared in about two weeks. Gonococcal peristasis a week or two longer in the stained smear while the patient is continued on estrogens. If a child is followed until the smear becomes negative the danger of infection and the danger of recurrence of the highly infected discharge has passed. By the end of one year the disease has usually been cured spontaneously. If not by the action of the drug used.

HENRY C. FALK, M.D.

MISCELLANEOUS

Leatham, J. H., and Abarbanel, A. R.: Gonadotropins and the Antihormone Problem. *West. J. Surg.* 94:4, 5, 491.

The authors note that the combination of extract from the anterior pituitary lobe of the sheep and human chorionic gonadotropin (synapoidin) has received little consideration with regard to its antigenic activity. Investigators have reported a negative test for antigens to this hormone combination in 1 patient. Other investigators have noted allergic manifestations following hormone administration. It is generally agreed that chorionic gonadotropin is not antigenic in the human being. From reports given, one can assume that the chorionic gonadotropin in synapoidin is not antigenic. However, the material also contains extract of the anterior pituitary lobe of the sheep which potentially could be antigenic. There are very few reports in which anterior pituitary lobe extracts have been administered clinically and in which tests for antigonadotropins have been made.

It seemed desirable to the authors to investigate further the question of antigonadotropins in patients treated with synapoidin. The results of 3 cases are presented and herewith reported. The methods used in these studies are described. The serum of each patient was tested for antigonadotropins against synapoidin before the hormone treatment was begun and no antagonistic substance to this combination of gonadotropins was detected. During the course of therapy with synapoidin, sera tests were performed at various intervals from the time of the first injection. A detailed tabulation of the test data obtained from 2 of the patients is shown.

Antigonadotropic substances were not detected in the sera from 3 patients injected with a combination of extract of the anterior pituitary lobe of the sheep and human chorionic gonadotropin. The maximum period of hormone administration was five months. No allergic manifestations were noted and skin tests were negative. The sera of 6 amenorrheic women were tested for antagonists to synapoidin prior to therapy. All tests were negative.

HENRIET F. THURSTON, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Sesley W F: A Study of 250 Cases of Placenta Previa. *Am. J. Obst.* 1945 49 85

For a ten-year period from 1933 to 1942, there were 31,956 deliveries at the Harper and Herman Kiefer Hospitals, Detroit Michigan among which there were 250 cases of placenta previa, 1 in 128. Placenta previa is found in primiparas and multiparas in the ratio of 1 to 5. It is more common in white persons than in colored. It occurs most commonly in the middle childbearing age.

A high percentage of twin pregnancies and fetal malformations is to be expected among cases of placenta previa.

A large group of such cases was satisfactorily managed by expectant treatment during the stage of dilatation or by simple rupture of the membranes.

The insertion of the dilatable bag gives good results in cases adapted to its use.

In properly selected cases cesarean section can be used to the advantage of both mother and child.

Seventy five per cent of the cases in which roentgenography was used were correctly diagnosed by this means.

Blood transfusion should be available to all patients with placenta previa. An acceptable mortality rate cannot be expected without it.

The maternal mortality in 250 cases of placenta previa taken from a large metropolitan area was 2.3 per cent. The gross fetal mortality was 34.6 per cent the net, 14.4 per cent.

EDWARD L. CORNELL, M.D.

Allen, E. D.: Pregnancy and Otosclerosis. *Am. J. Obst.*, 1945 49 32

Attempts to collect data have convinced the author that difficulties in hearing during pregnancy are frequently overlooked, neglected entirely and often inadequately studied. A very careful family history concerning deafness should be taken of every pregnant woman who experiences appreciable changes in hearing.

For progressive deafness to be considered an indication for therapeutic abortion, a definite diagnosis of otosclerosis must first be made.

Definite otological evidence should be obtained and preserved before, during and following pregnancy and lactation for evaluation concerning succeeding pregnancies.

Otosclerosis should probably not contraindicate marriage or a trial pregnancy.

Otosclerosis should not be considered as an indication for therapeutic abortion in the primipara.

Deafness need not be present, but a familial history of deafness may be one of the deciding factors for the interruption of pregnancy. A multiparous woman may have considerable right to question

the continuation of her pregnancy if accurate otological evidence obtained in previous pregnancies has shown a marked *sustained* loss of hearing.

Before therapeutic abortion is decided upon the patient should be informed that otosclerosis is a progressive disease even without pregnancy also that hearing aids and lip reading offer great help.

Fetuses in all stages of development born to mothers with decreased hearing should be preserved for examination by a competent otological pathologist. This applies especially to twins.

EDWARD L. CORNELL, M.D.

PUERPERIUM AND ITS COMPLICATIONS

Dingle, P.: Prophylactic Use of Pneumoperitoneum in the Puerperium of Tuberculous Patients. *J. Obst. Gyn. Brit. Empire* 1944, 51 499.

The present accepted treatment of tuberculous patients who become pregnant has been to induce an abortion up to a period of four months. More advanced pregnancies are permitted to proceed to term because the results of late abortion are as serious as those of pregnancy at term. During the past two years it has been possible for the author of this report to study a series of 30 consecutive cases of patients suffering from pulmonary tuberculosis. These patients were not seen in either the tuberculosis clinic or the antenatal clinic until after they were well into the fifth month of pregnancy.

The treatment of these patients consisted of

1 A sufficiency of rest, food, and fresh air during the antenatal period. pneumothorax was used when indicated.

2 The first stage of labor was made as comfortable and as easy as possible by the administration of suitable drugs. the second stage was shortened and the strain reduced by an episiotomy or by the use of forceps.

3 In the puerperium, a pneumoperitoneum was induced within one hour of delivery by the inflation of 3,000 cc. of air or air-oxygen mixture into the peritoneal cavity. one week later 2,000 cc. were given, and after a period of one more week, 1,000 cc. were given. The mother was put on complete bed rest and did not feed her infant by breast except in 1 or 2 instances.

Thirty cases were studied. In the first group there were 4 with a positive sputum and bilateral active disease. 2 had a hopeless prognosis, and of these, one died and the other was seriously ill. the remaining 2 were greatly improved at the end of six months. In group 2 also consisting of 4 patients having a positive sputum with unilateral disease. 1 was unco-operative and died. the 3 others are making satisfactory progress. Group 3 comprised 2 patients with active disease, as was shown by x rays but with negative sputum and both showed im

provement after a period of six months. Group 4 totaled 8 patients with unilateral disease, all of whom were progressing satisfactorily after a period of six months. Group 5 consisted of 3 patients who had a thoracoplasty seven and ten years respectively prior to delivery and the condition of both remained satisfactory. Group 6 comprised 3 patients with pleurisy only both patients were benefited. Group 7 comprised 3 patients with a phrenic crush, or an avulsion 1 progressed satisfactorily and 1 was too recently delivered to permit an evaluation. Group 8 comprised 6 patients with quiescent, or healed disease all were benefited.

The final observation in this study was that of the 30 patients, 25 passed through labor and the puerperium and are doing well 5 more are in the early puerperium. The author concludes that the use of pneumoperitoneum is advocated as a prophylactic measure in the treatment of tuberculous patients in the puerperium.

SAMUEL J. FOGELSON M.D.

MISCELLANEOUS

Jones, G. E. S., Delfs, E., and Struss, H. M.: Chorionic Gonadotropin and Pregnanadiol Values in Normal Pregnancy. *Bull. Johns H. Mem Hosp.* 1944 75 359.

The authors have studied the chorionic gonadotropin serum levels and urinary pregnandiol values of 18 women throughout normal pregnancy. In an additional 6 women the chorionic gonadotropin levels only were studied. Two cases of twin pregnancy were also observed for chorionic gonadotropin only 1 of them being observed for pregnandiol.

The findings revealed that the curve for serum chorionic gonadotropin rises precipitously reaching a peak between fifty and sixty-five days from the first day of the last menstrual period. The level then declines gradually until about the 100th day then a still more gradual decline for the next thirty days, and finally the level is maintained low until the end of pregnancy. There is a slight hint of a secondary rise between the 100th and 130th days, but this is probably unimportant.

The actual levels in this study started at about 3,000 I.U. per liter and rose to a peak of 150,000 I.U. per liter gradually declining to between 10,000 and 15,000 I.U. and finally to between 1,000 and 6,000 I.U.

The amount of free pregnandiol in the urine of pregnant women was calculated in milligrams per twenty-four hours. The pregnandiol excretion curve can be divided into 3 periods: that in which the corpus luteum is the main source of progesterone production and that in which the placenta is probably

the most important site of progesterone formation. During the first period which ends between the sixty-fourth and seventy-eighth days, the pregnandiol values are rarely above 30 mgm. or below 6 mgm. per twenty-four hours. Throughout the remainder of the pregnancy there is a gradual rise in the pregnandiol-excretion curve until about the 350th day when the peak values are attained. The average peak value was 85 mgm. per twenty-four hours.

Two cases of multiple pregnancy were observed. One showed abnormally high chorionic gonadotropin values maintained throughout pregnancy while the other showed only moderately high values in the first half of gestation and a normal curve in the second half of pregnancy.

The pregnandiol studies in the one case of twins in which they were observed revealed figures compatible with those found in the women with single pregnancies.

There was a rather wide individual variation in the cases studied, but a very definite average was demonstrable.

HARRY FINE, M.D.

Halbrecht, L.: Artificial Insemination (Report on 80 Cases). *J. Obst. Gyn. Brit. Empire*, 1944, 51: 556.

The indications for the adoption of artificial insemination were divided into three groups:

1. Defective spermatozoa
 - a. Severe oligospermia
 - b. Necrospemia
 - c. Faulty germ plasma
 - d. Azoospermia
2. Anomalies of the male external genital organ
3. Sterility without evidence of its cause in either of the partners

Azoospermia and severe oligospermia were considered as absolute causes of sterility.

The intrauterine and intracervical techniques were used. The former was abandoned because of technical difficulties and unnecessary risks, except when stenosis and atresia of the cervix were present.

Two unsuccessful attempts at insemination were made with refrigerated spermatozoa and 3 others with aspirated testicular material from husbands suffering from obstruction of the genital passages due to gonorrhea.

Three or four inseminations were made between the twelfth and eighteenth days for from 3 to 6 cycles. The donors were selected with the usual precautions.

In 23 of 53 cases of sterility associated with defective sperm pregnancy occurred. Of 18 patients to whom the husband's semen was used, 3 became pregnant.

JAMES F. DONNELLY M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY AND URETER

Warren F. L.: Estimation of Urinary 17 Ketosteroids (a) Adrenal cortical tumors in the male and female (b) pituitary basophilism adrenal virilism or hirsutism in the female without tumor (c) pubertal virilism in female children without tumor and (d) miscellaneous conditions such as carcinoma of the breast, seminoma of the testis, and so on. Data are given for 92 patients studied by the author as well as for 20 cases of adrenocortical tumor reported previously by others.

The author presents an extensive review of the levels of the urinary 17 ketosteroids in the following conditions: (a) adrenal cortical tumors in the male and female (b) pituitary basophilism adrenal virilism or hirsutism in the female without tumor (c) pubertal virilism in female children without tumor and (d) miscellaneous conditions such as carcinoma of the breast, seminoma of the testis, and so on. Data are given for 92 patients studied by the author as well as for 20 cases of adrenocortical tumor reported previously by others.

The values found in the 4 cases of adrenocortical carcinoma studied by the author ranged from 83 to 690 mgm per day. The majority of values found by other workers were in this range. For the group of individuals all female, classed as cases of pituitary basophilism adrenal virilism or hirsutism without adrenal tumor, the range of values reported by the author was from 3.4 to 37 mgm per twenty four hours, with a mean value for the three groups of 18.6, 22 and 16 mgm. These values are in nice agreement with those reported by Crooke and Callow and others for similar patients. Cases of pubertal virilism in female children showed a range of from 8.4 to 100 mgm. per day. Again these values of the author were in agreement with the findings of other investigators.

In addition to analytical data problems arising in the clinical differential diagnosis of the aforementioned conditions are discussed and evidence is added to that of Crooke and Callow as well as of others that the differentiation of adrenocortical tumor may be made by estimating the greatly increased excretion of urinary 17 ketosteroid particularly the beta fraction. Excretion in cases of proved tumor are usually well above the range for conditions such as pituitary basophilism but an intermediate zone exists in which interpretation is difficult. However in the cases cited in which separations are reported, dehydroisoandrosterone in large amounts was found only in patients with adrenocortical carcinoma. In 2 cases of pubertal virilism in children with values for total 17 ketosteroid between 90 and 140 mgm, large amounts of androsterone were isolated. Dehydroisoandrosterone was either absent or present in an amount too small to be isolated.

DONALD F. McDONALD M.D.

Dodge, H. J. and Benner M. C.: Neuroblastoma of the Adrenal Medulla in Siblings. *Rocky Mountain M. J.*, 1945 43 35

Although sufficient cases of tumors of the sympathetic nervous system particularly neuroblastoma

mas, are now on record so that distribution as to age, sex, race and primary site of development is well established there are only two references to a familial incidence of these tumors in the English literature and no proved cases on record.

The authors present case histories and pathological data of 2 siblings, one a four year-old female and the other a seven month-old male who died with neuroblastomas of the right adrenal gland. The presenting complaint was abdominal enlargement in both cases. In the older child a mass appeared two months following the initial abdominal enlargement, whereas in the infant a very large mass was found on first examination. The clinical course of the disease was short.

Only a few weeks in the infant and three months in the four year-old child. Pathological examination revealed only local extension of the tumor in the older child but there were extensive hepatic metastases in the infant. A third child of this marriage, now one year old is apparently free of the disease.

The infrequency of familial neuroblastomas derived from the sympathetic system is reflected in the lack of recorded proved cases in the literature. It is believed that this is the first adequately proved instance of familial neuroblastoma.

DONALD F. McDONALD M.D.

Smith E. C. and Orkin L. A.: A Clinical and Statistical Study of 471 Congenital Anomalies of the Kidney and Ureter. *J. Urol. Balt.* 1945 53 1

Malformations of the kidneys and ureters are of great clinical importance and account for about 40 per cent of all pathological conditions akin to these organs. They can be diagnosed by complete urological investigation especially excretory urography.

In a large series of 18,460 consecutive urological admissions, the authors found 471 instances of congenital anomaly. The incidence according to this data would be 1 to 40 but this is much too low. Since the introduction of excretory urography in the authors' hospital the incidence has been found to be 1 to 27 (3.7 per cent).

While the most frequent congenital anomaly is that of double renal pelvis and ureter which occurred 97 times, or a clinical incidence of 1 to 190 the other anomalies occur frequently enough to warrant attention.

A consideration of the individuals in this series shows that the average age was thirty-seven years that males were slightly more affected than females the ratio being 250 to 221, and that there was no apparent predilection for either the right or left side. Considered together unilateral involvement is at least four times more frequent than bilateral involvement.

Although anomalies are compatible with a healthy existence this is the exception rather than the rule.

as this occurred in only 17 per cent of the cases. Practically any urological symptom may be encountered but the most frequent is that of pain which occurred in 78.9 per cent of the cases. A further study of symptomatology reveals that the anomalous kidney may produce symptoms without the presence of associated renal disease.

In the series of anomalies, only 20.5 per cent showed no associated pathological changes to illustrate the point that the malformed kidney is especially prone to disease. Considered together urinary infection, hydronephrosis, and calculus accounted for 89 per cent of the secondary pathological findings in these cases.

In this study 138 cases (30.3 per cent) required open surgical intervention for the relief of this condition, which was almost equally divided between the operation of nephrectomy and conservative procedures.

Since congenital anomalies have been shown in this article to be especially prone to disease, it is believed that only by early diagnosis and treatment can a good many of these complications be prevented or ameliorated. And with the use of chemotherapeutic agents, the ease and ability to perform conservative and plastic procedures will certainly increase in the instances of congenital anomalies that come to open operation.

JOSEF A. LOSEY, M.D.

Cooley T. F. and Walker J. H.: Congenital Solitary Kidney: Case Reports and Consideration of Military Significance. *J. Urol.*, Balt., 945 534

The recognition of congenital solitary kidney during life has been made possible by the use of pyelography. The incidence of the anomaly must be in the neighborhood of 1 in 1,000 as judged from autopsy reports. Criteria for diagnosis are (1) absence of the renal silhouette on the abdominal flat film (2) roentgenological evidence of renal enlargement and (3) possible asymmetry of the psoas shadows, (4) absence of opaque media on the agraphic side on the ureteral excretory urography (5) absence of the ureteral orifice on one side after repeated cystoscopic examination in an otherwise normal appearing bladder and (5) absence of indigo-carmin elimination on the affected side. A sixth corroborative criterion is an associated abnormality of the genital tract, which is far more common in the female because of the later development of the müllerian system.

The authors present a case of sulfadiazine crystalluria and oliguria in a twenty-six year-old male who had received 84 gm of sulfadiazine in eighteen days as treatment for gonorrheal urethritis. Investigation of the upper urinary tract revealed a congenital solitary left kidney. A second case, that of a twenty-nine-year-old male complaining of frequency, urgency, and nocturia of ten years' duration, is reported. He also complained of right sacroiliac pain of three years duration. Physical and urological findings of significance were lumbar scoliosis, bilateral pes planus, left varicocele, and a well

marked prostatitis. Laboratory findings were normal. Urinalyses were normal and excretory pyelograms and cystoscopy showed a congenital solitary left kidney.

The authors conclude that the anomaly is generally silent and clinical recognition most frequently results from an incidental investigation. The relative frequency of occurrence and the finality of the error if a single kidney be removed makes it essential that pyelography be performed prior to any surgical procedure upon the upper urinary tract. The incidental discovery of the anomaly when the solitary kidney is normal is neither an indication for resection nor an adequate cause for discharge of a patient from military service.

DONALD F. McDONALD, M.D.

Frien E. L. The Mechanism of Renal Complications in Sulfonamide Therapy. *N. England J. M.* 945 23 63

Renal complications to sulfonamide therapy continue to occur despite an increasing experience and the use of the more soluble sulfonamide drugs. The usual mechanism that produces these complications is the obstruction of the urinary channels by insoluble concretions composed principally of the acetyl derivatives of the drugs. Less frequently a toxic injury of the tubules, independent of concretions, produces anuria and uremia. In such cases the only lesion in the urinary tract may be a widely disseminated focal necrosis affecting the kidney tubules.

Two cases of sulfathiazole anuria and uremia are reported. No obstructing concretions were encountered in the ureters or kidney pelvis by cystoscopy and pyelography. Renal decapsulation was done and cortical biopsies were taken. One patient died, and the other recovered rapidly, apparently as a result of decapsulation. There were no crystals or concretions in the kidney tissue taken by biopsy nor in the entire urinary tract (including the kidney tubules) of the fatal case that came to autopsy. A rigorous technique that precludes the loss of drug crystals in preparation of the tissues is described.

The most important factor in the causation of renal complications is a low urinary output.

The development of obstruction concretions depends on two physical conditions—the hydrodynamics of the urinary tract and the affinity of crystals for each other.

Crystals of the sulfonamides first form in the convoluted tubules, where reabsorption of water occurs. Sedimentation of these suspended crystals occurs in the terminal portions of the collecting tubules and in the renal calyx. Proximity of the crystals here results in aggregation and the formation of concretions that obstruct the terminal portions of the collecting tubules. This process progresses in a retrograde manner upward in the collecting tubules. Calyces concretions remain in situ or pass down the ureter much as do ordinary urinary calculi.

DONALD F. McDONALD, M.D.

It has been only in the past twenty years that the realization of the fact that gastrointestinal symptoms may predominate in cases of malignancy of the kidney has been reflected in the literature. That these symptoms are related to the common innervation of the gastrointestinal tract, the kidney and the ureter has been attested by anatomists, clinicians, and researchers.

In order to assess the possible value of the type of gastrointestinal symptoms the frequency of occurrence, and the possible relationship to the histological type of the renal tumor a study of all proved renal tumors at the Beth Israel Hospital New York, was made. In five years 33 cases of which 22 occurred in men and 11 in women were found. There were 22 hypernephromas (65 per cent) of which 10 were presented with only gastrointestinal symptoms. In the remaining 11 cases the patients complained of hematuria. Tumors of the renal pelvis occurred in 6 cases, or 17 per cent, and all of these presented only urological symptoms, usually painless hematuria. There were 3 cases of renal carcinoma in none of which was there ever any positive urinary symptoms or findings. These 3 cases were explored with the possibility of ovarian or gastrointestinal neoplasms in mind. There was 1 case of lipoma of the kidney and 1 case of retroperitoneal tumor of undetermined histopathology in which gastrointestinal symptoms predominated.

There was found to be no differential value to the type of gastrointestinal symptom associated with renal tumors which would distinguish between gastrointestinal and renal disease. In all 3 cases of renal carcinoma there was no urologic complaint. In all cases of tumor of the renal pelvis there were urologic symptoms without any gastrointestinal symptoms. Twenty three of the series or 69 per cent, had gastrointestinal symptoms and a fair number showed no urologic findings.

It is suggested that any cases presenting disturbing abdominal symptoms with negative findings should have a complete urologic investigation.

DONALD F. McDONALD, M.D.

Abeshouse, B. S. and Weinberg, T.: Malignant Renal Neoplasms; A Clinical and Pathological Study. *Arch. Surg.* 1945 50 46.

A study of 63 renal neoplasms observed during the past twenty years, and a review of the literature warrant the following conclusions.

Renal neoplasms are more common in men than in women. They occur with equal frequency in each kidney. Parenchymal renal neoplasms occur most frequently in the sixth and seventh decades of life, with the exception of the Wilms tumor which occurs in early infancy and childhood.

The most common initial symptom is painless hematuria. Next in frequency are pain and a tumor mass. The classic symptom triad which may be ob-

served during the course of the disease is found in the following order of frequency: pain 94 per cent, hematuria, 81 per cent, and tumor mass, 63 per cent. This symptom triad is usually reversed in children with Wilms tumor and in inoperable adults in whom a mass is usually the most prominent symptom.

Retrograde pyelographic studies were performed in 56 cases, and a correct preoperative diagnosis, based on the pyelographic findings was made in 42 cases. Greater reliance should be placed on retrograde pyelography than on intravenous urography in the diagnosis of renal neoplasms. The most common urographic findings in order of frequency are compression of one or more calyces, elongation of one or more calyces, distortion or compression of the pelvis, displacement of the ureter or the pelvis dilatation of the pelvis, and calcification within the tumor. In parenchymal neoplasms, the characteristic change is compression, elongation, or obliteration of one or more calyces. In pelvic tumors a filling defect of the pelvis is the most common finding.

Among 53 cases treated by nephrectomy there were 4 deaths. Surgical intervention is justifiable in every case of suspected renal neoplasm. Early diagnosis and operation increase the chance of cure.

The prognosis is influenced by the nature and duration of the symptoms, the condition of the patient, the type, size, and mobility of the tumor, the presence of tumor thrombi in the renal vein and in the inferior vena cava, the presence of metastases, the type of surgical treatment, and irradiation therapy.

The best results following nephrectomy from the standpoint of survival were obtained with Grawitz tumors. The poorest results followed operation for pelvic neoplasms.

SAMUEL KAHN, M.D.

Percival, R. C.: Ureteral Calculus Treated by Reversed Catheterization. *Lancet*, Lond., 1945 248 15.

The ureteral calculus, recently impacted and showing no sign of progress under observation, is not rare. Several procedures for dealing with such calculi have previously been described but no one method is sufficiently reliable to merit use routinely.

A simple and effective method of extracting a small recently impacted calculus is described. The principle of the method is gradual ureteral dilatation through intermittent traction on a ureteral catheter made to form a loop which grips the stone. In 50 cases reported by Finney and in the 3 cases reported by the author no complications of any kind were encountered.

SAMUEL KAHN, M.D.

Vest, S. A.: Conservative Surgery in Certain Benign Tumors of the Ureter. *J Urol* Balt., 1945 53 97.

Treatment of all types of ureteral tumor whether benign or malignant, has usually consisted of removal of the kidney and ureter. So far as the writer is aware, not one author has indicated in his report any evidence of metastases following treatment of benign ureteral tumors. Many authors have been questioned



Fig. 1. Showing villous and sessile papilloma composed mainly of epithelial tissue. The cells are well differentiated and tend to become polygonal and flat near the surface. There were no mitoses and absolutely no invasion of the basal membrane. This characteristic appearance was confirmed throughout the other sections.

but no reports of recurrences have been received. The author believes from the study of previously reported cases in the literature and his own experience that benign and nonmetastasizing tumors do occur and, when favorably situated and properly diagnosed, can be treated conservatively. Three cases are reported and the writer believes from a standpoint of the previous history, the clinical and pathological findings, and the course since operation, that the lesions can be considered as benign tumors.

Case 1 was that of a sixty-three-year-old male with a history of symptomless hematuria of one week's duration. Four months previously he had had renal colic on the right side without calculi or hematuria. Cystoscopy of the bladder was essentially normal with the exception of a small papillary tumor about 1 by $1\frac{1}{4}$ cm. in size which obscured the right ureteral orifice. A ureteral catheter was passed to the left kidney with ease on the right side it went through the middle of the tumor to the kidney. X-ray showed a normal kidney and ureter on the left, but on the right side there was considerable dilatation of the ureter and kidney pelvis with an irregular filling defect in the lower ureter. Biopsy showed the tumor to be benign and papillary in character. The pyelogram indicated no evidence of tumor elsewhere in this ureter or the kidney pelvis. At operation when the ureter was opened a large papilloma extruded the tumor was readily lifted out of the ureter and found to have a base with a diameter of from 1 to $1\frac{1}{4}$ cm. It came off abruptly from the normal mucosa with no puckering induration and no evidence of invasion. The ureteral wall was soft and pliable and there was not the slightest suggestion of malignancy. The tumor was excised with a wide margin of ureteral wall around the base following which the ureter was sutured with continuous fine

catgut. The pathological study (Fig. 1) revealed a papillary tumor with uniform cells and no mitoses or invasion of the basement membrane. For the past seven and one half years the patient has returned for periodic observation. He has had no urinary symptoms and no hematuria. Pyelograms have shown no evidence of recurrence.

Case 2 was that of a fifty-two-year-old male with a history of painless hematuria of eight days duration. Cystoscopy showed a normal bladder and ureteral orifices, both of which ejected urine in the usual manner. The urine from the left was bloody. A catheter was passed to the right kidney with ease but on the left side the catheter would not pass the region of the midureter. Plain x-rays were normal. The pyelogram was normal on the right side, while on the left the lower ureter showed a beginning dilatation just above the brim of the pelvis. Opaque media filled the spindle-shaped dilatation up to a certain point at which it abruptly stopped. Intravenous x-rays showed a normal ureter on the left side except for a spindle-shaped dilatation of the midureter. When the ureter was exposed at operation there were no extrureteral masses, adhesions, obstructions, or induration. The ureter was opened longitudinally over the dilated portion and a black spindle-shaped mass about $1\frac{1}{4}$ cm. in diameter and 4 cm. long was removed. It was bulbous below and running out into a fine filamentous termination above. Frozen section of the ureteral wall showed only hypertrophy of all layers. Frozen section of the mass disclosed a papillary necrotic tumor which seemed to be benign. The tumor was lying loose in the ureter and above this section a small area of thickening in the ureteral wall could be felt. This was the previous point of attachment of the papilloma and was removed together with a margin of the surrounding normal wall of the ureter. A frozen section of this base of the new growth revealed an apparently benign papilloma (Fig. 2) only the mucosa was involved with no evidence of infiltration. No other evidence of any more papillomas could be found or felt in the pelvis of the kidney or the remainder of the ureter. The ureter was, therefore, closed over a small catheter by an end-to-end anastomosis with four sutures of No. 0000 chromic catgut. This patient has been followed from time to time with both intravenous and retrograde pyelograms, all of which have been entirely normal; there has been no hematuria or urinary symptoms and the urine on repeated examination has never shown red blood cells.

Case 3 was that of a fifty-nine-year-old Army medical officer who had undergone frequent fulgurations since 1908 for hematuria and a papillary tumor emerging from the right ureteral orifice. In 1937 the pyelogram showed normal kidneys with a dilated right lower ureter and a filling defect. At this time the tumor was fulgurated with the aid of a small meatotomy. At the operation in 1943 the ureter was found to be dilated from about the brim of the pelvis down to the bladder. It was opened with a longitudinal incision and a single papillary tumor was



Fig. 2. Pathological study a, Left Section of urethral wall including tiny base or origin of pedunculated tumor. Urethral wall is entirely normal in appearance. Base of the papilloma is composed of small, thin, spindle-shaped cells with absolutely no evidence of invasion. Section at

other levels of this area confirms these findings. b, High power magnification of papilloma base. Transitional epithelial cells are uniform and do not appear malignant. There are no mitoses. (Section of the large papilloma in this case showed it to be necrotic.)

found on the posterior wall. Just above the bladder were five small structures apparently fresh implants. The pedicle of the tumor was narrow and could be moved freely with the mucosa. It seemed probable to the operator that this was a tumor which was non-invasive and involved only the mucosal layer of the urethral wall; this seemed to be true also of the tiny implants. The papilloma was grasped with forceps and the pedicle divided cleanly at the base. This

left a defect in the mucosa which exposed clean musculature and absolutely not the slightest evidence of infiltration. The lower implants were fulgurated following which the urethral incision was carried almost to the bladder to make sure no implants existed in the intramural ureter. Frozen section (Fig. 3) convinced the operator that this was a benign papilloma of some twenty five odd years of duration. The ureter was then closed with continuous fine cat



Fig. 3. Pathological study a, Left Papillary tumor and epithelial cells which do not differ greatly from normal transitional epithelium. In many places they are only 5 to 6 cells deep. The stroma is made up of loose vascular connective tissue. The basal membrane is uniformly even and there is not the slightest evidence of invasion. b, High

power magnification illustrating uniformity of the epithelial cells and absence of any mitoses. The cells are well differentiated and tend to reduplicate normal mucosa. It is of interest that this tumor had been present for approximately twenty-eight years.



Fig. Showing villous and sessile papilloma composed mainly of epithelial tissue. The cells are well differentiated and tend to become polygonal and flat near the surface. There were no mitoses and absolutely no invasion of the basal membrane. This characteristic appearance was confirmed throughout the other sections.

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power magnification illustrating uniformity of the epithelial cells and absence of any mitoses. The cells are well differentiated and tend to reduplicate normal mucosa. It is of interest that this tumor had been present for approximately twenty-eight years.

gut. Fifteen months after operation the patient has had no hematuria or recurrence of the tumor. Cystoscopy shows no evidence of mental or other type of tumor and the ureterogram shows no evidence of filling defects. Further pathological study of the tumor showed a benign appearance and no indication of invasion.

In conclusion, therefore, it seems that surgeons should carefully consider any localized ureteral tumor from the clinical, x-ray, gross, and pathological aspects before they sacrifice the kidney. However any decision between nephroureterectomy and conservative management should be made by competent urological surgeons and pathologists.

JOHN W. BRENNAN, M.D.

Jewett, H. J.: Ureterointestinal Anastomosis In Two Stages for Cancer of the Bladder. *J. Urol.*, Balt., 1944, 53, 136.

The accumulated experience of the last thirty years has shown that a number of uncontrollable factors may arise after the Coffey operation and nullify the effects of a perfectly executed procedure. Therefore the author attempted to develop a method which would reduce these uncontrollable complications to a minimum, and would give consistently good results when properly executed.

His two-stage procedure had its inception in the experimental laboratory. None of the author's dogs survived any appreciable time after bilateral transplantation by the Coffey method, but after bilateral transplantation by this two-stage method, the dogs recovered rapidly and survived for indefinite periods. One can hardly fail to see the existence of an added factor of safety afforded by the two-stage principle, which allows the newly implanted ureter to heal as a graft in an aseptic bed before complete communication is established. This factor of safety is sacrificed in the Coffey operation.

The results in the series of 33 cases, completed during the last four years have demonstrated the soundness of the basic principle involved in this two-stage method of ureterointestinal anastomosis. When properly executed, subsequent hydronephrosis has been the exception rather than the rule and even in those instances in which some dilatation did occur ascending infection has been infrequent, if it did not exist prior to ureteral transplantation.

The author modified his original technique. The implantation is made exactly as originally described, except that the seromuscular flaps are approximated over the imbedded ureter by interrupted sutures of No. 0000 chromic catgut, with an atraumatic needle, instead of by continuous suture. (The latter sometimes caused a shortening of the bed.) The sutures should be drawn fairly taut, so that a naked strand of catgut will not cut into the underlying ureter and cause urinary extravasation. One must avoid piercing the intestinal mucosa with the needle, and compressing or constricting the ureter at any point. Adhesions causing rigid fixation of the sigmoid (containing the implanted ureter) to the poste-

rior pelvic wall have been much reduced by a modification of the original technique of the first stage. Some fixation of this portion of the sigmoid is desirable, in order to prevent kinking, stretching, and twisting of the ureter. Complete fixation, however, as originally advocated, by extraperitonealization of the site of implantation is unnecessary and in some cases has made adequate mobilization and delivery difficult at the second stage. The principal modification of the technique of the first stage consists in the abandonment of this extraperitonealization. Adequate immobilization is accomplished by apposing the serosa of the bowel to the serosal surface of the posterior parietal peritoneum. Adhesions thus formed are readily separated at the second stage.

The author emphasizes the following important facts: (1) a thorough search for metastasis should be made before operation, and chest films must be accurately interpreted; (2) excessive traction of the emerging ureteral stump must be avoided; (3) the patency of the ostium must be properly tested; (4) the ureteral stump must be adequately secured; (5) preoperative deep x-ray therapy may make closure of the peritoneum after cystectomy impossible; (6) preoperative renal infection may cause fatal urosepsis after transplantation, and (7) patients should not retain urine in the bowel longer than four hours, and should have satisfactory movements each day.

Modification of the operative technique of the two-stage method of ureterointestinal implantation has simplified the procedure.

The most important measures to be adopted at the first stage are: (1) prophylaxis of adhesions; (2) proper fixation of the sigmoid containing the ureter—at the second stage: (a) adequate mobilization of the sigmoid containing the ureter; (b) calibration of the intramural ureter; (c) avoidance of tangential cut with electrodes; (4) establishment of ostium of adequate length; and (5) prevention of subsequent leak from emerging ureteral stump by treatment with phenol and alcohol and by triple ligation.

No statement is made in regard to ultimate cure because less than five years have elapsed since total cystectomy in all of the cases of carcinoma of the bladder.

JOSEPH K. NARAT, M.D.

BLADDER, URETHRA, AND PENIS

Hess, E., and Wright, B. W.: Pyelocystostomosis: Report of Two Cases. *J. Am. M. Ass.* 1943, 137, 267.

The authors report 2 cases of direct anastomosis of the kidney pelvis to the urinary bladder—the first in a boy nine years old who had a huge hydronephrosis in the left half of a horseshoe kidney which could not be relieved with the cystoscope. Fourteen years later he was perfectly well with a normal urinary output and had no symptoms.

The second case in a patient of forty-two was diagnosed as hydronephrosis in a congenital ectopic

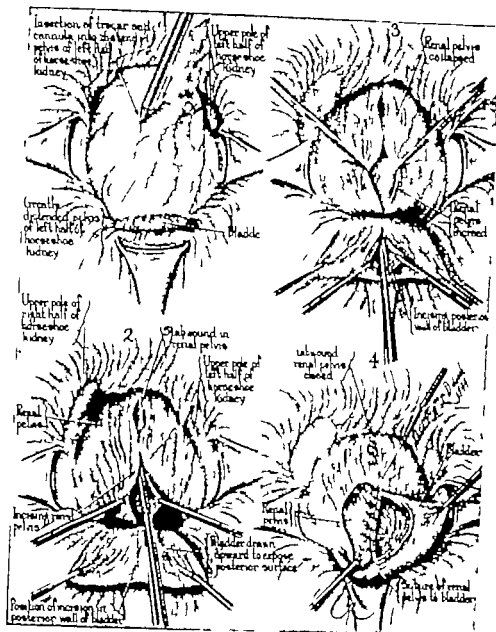


Fig. 1. 1 Bladder and hydronephrosis exposed through a midline incision. 2 Line of incision in the posterior wall of the bladder and the incision in the pelvis. 3 Relationship of the incision in the posterior wall of the bladder and the nephrotic pelvis. 4 Method of anastomosing the pelvis to the bladder.

solitary kidney. The condition was relieved by ureteral catheterization. Three weeks later the patient again had an acute hydronephrosis and 6 oz. of urine was drained from the hydronephrotic pelvis. Thirteen days later an attack of hydronephrosis was accompanied by severe colicky pain in the lower abdomen and suppression of the urine. The nonprotein nitrogen was 106.0 and the creatinine, 7.2 mgm. per 100 c.c. His blood pressure had risen to 210/110 as compared to 132/94. He had a severe headache, visual disturbance, vertigo, mental dullness and hallucinations with an obviously impending uremia.

At surgery, the ectopic kidney could be seen and felt beneath the posterior peritoneum in front of the first portion of the sacrum. A careful search failed

to reveal another kidney or a missing testicle. The right ureter was a blind pouch; the left ureter entered the hydronephrotic pelvis on its upper left anterior surface and was sharply angulated at the ureteropelvic junction. The long axis of the kidney was horizontal. The blood supply to the kidney was typical of that seen in ectopias and came from the abdominal aorta.

The posterior parietal peritoneum was incised in the midline and stripped from the kidney and the posterior wall of the bladder. The lower border of the renal pelvis was first attached to the lower part of the posterior wall of the bladder by several interrupted sutures of catgut, the purpose being to protect the anastomosis from undue tension. An extraperi-

last biopsy specimen was taken one hundred and twenty days after treatment with a total dosage of 1.145 mgm. of diethylstilbestrol given in average daily doses of 17 mgm.

The progressive changes depicted in this series of photomicrographs consisted of a proliferation of the epithelium of the ducts, the cells of the ducts increasing in their thickness from one to fifteen or more," and becoming elongated and finally portraying a process of budding—at times six or more buds could be found developing on the one duct which was present before treatment. There was also evidence of an increase in the connective tissue stroma, vascularity and periductal edema, and, finally in a section from another male breast, fat deposits were present, the subject having had 680 mgm. of diethylstilbestrol (an average of 1.4 mgm. per day for 485 days). The epithelium of the ducts along with its proliferations showed large cells of various shapes and sizes. The duct cells at times were multiplied to such an extent as to occlude the lumen, however

the cells were deeply staining and the basement membrane remained intact everywhere and was not invaded by the cells of the epithelial proliferative process. Indeed the authors stressed the fact that they had as yet observed no malignant changes in the breast from treatment with diethylstilbestrol and rather doubted if they would ever be found.

In concluding, the authors stated that the breast enlargement grossly as well as the breast proliferation microscopically is no indication as to the amount of benefit the patient is receiving with regard to the cancer of the prostate gland, and that the breast changes, although not serious in themselves are dangerous in that the patient often stops taking diethylstilbestrol when the breast pains begin or when they become severe. As yet the authors have observed no patient who was benefited more by orchiectomy than by the administration of diethylstilbestrol; they reserve the surgical procedure for those not benefited by endocrine therapy.

JOHN W. BARNHAM, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC

Dickson F D: The Clinical Diagnosis, Prognosis, and Treatment of Acute Hematogenous Osteomyelitis *J Am Med Ass* 1945 127 212

The prognosis and treatment of acute hematogenous osteomyelitis is discussed with the view that actually two separate and different syndromes are labeled with the same name. Both types of acute hematogenous osteomyelitis are initiated by a bacteremia and, in accordance with the course which the bacteremia takes, three different results may occur (1) the organisms in the blood stream may be destroyed (2) the organisms may lodge in bone, localize, and set up an osteomyelitis and (3) the bacteremia may become a septicemia with the formation of multiple abscesses in the lungs, kidneys, spleen, liver and the bones.

No matter under what circumstances organisms (staphylococci, streptococci, pneumococci) find their way into bone, a destructive process is set up. The reason why these abscesses occur predominately in the metaphysis of the bone is not known. The theory that multiple traumas are responsible for this occurrence proved to be incorrect. Fraser stated that in this area a great amount of reticuloendothelial tissue is found and as this acts as a defense mechanism, an infection is forced to localize in this area. Once the bacteremia has localized in bone areas, endotoxins are liberated and they destroy red cells, coagulate plasma, and cause the death of leucocytes. Because of the lack of the elasticity of bone the process spreads rapidly. A thrombosis of vessels occurs and there is less opportunity for the leucocytes to wander to this region to overcome the infection. Because of proteolytic toxins, the bone is autolyzed and partially destroyed and therefore, dead bone is found in these areas.

The clinical picture varies with the type of acute hematogenous osteomyelitis. Predominately children or adolescents are affected. In the usual case the first symptoms are pain, stiffness, and limitation of motion of the affected part. The temperature rises to between 102 and 104 F with a pulse rate of from 120 to 130 per minute. Restlessness and exhaustion due to the associated toxemia occur. Dehydration might occur with a persistently high temperature and decreased fluid intake. Localization of the process sooner or later occurs, and the affected region becomes swollen, hot, red and edematous.

The second type is initiated with a chill, and a rapid rise of temperature and delirium very frequently develop. These patients suffer from a septicemia with an associate formation of abscesses in various organs of the bones. Abscesses in bone seem to be only incidental to the existing pyemia. The

laboratory findings are characterized by a leucocytosis with a cell count ranging from 15,000 to 20,000. In most of the cases the blood culture is positive and anemia develops in the later stages of the disease. The antitoxic titer for staphylococci is important for the estimation of the natural defense of the patient and is found to be high in chronic osteomyelitis. It usually is higher in adults and rather low in infants. In making the diagnosis of acute hematogenous osteomyelitis, pyarthrosis, cellulitis, and in some instances, rheumatism have to be considered.

The prognosis of acute hematogenous osteomyelitis depends upon the type. In the first type the prognosis is good. In the second type the mortality is 50 per cent, perhaps higher. As far as the local bone focus is concerned age is the important factor. A great majority of patients three years or older pass on to the chronic stage. In infants the disease has very little tendency to become chronic.

At the present time there is considerable controversy as to the proper treatment of acute hematogenous osteomyelitis. This confusion exists because up until the present time no one tried to differentiate these two definitely different groups. In the first type the picture is that of a local infection associated with concomitant constitutional symptoms. In infants, that is, in children under two years of age, the treatment should be conservative and the general care of the patient rather than the osteomyelitis is the important consideration. With the use of sulfonamides, penicillin, and antistaphylococcus serum the disease quite readily becomes localized. The delicate periosteum usually breaks and the pus escapes into the surrounding tissues. If indicated, a small opening is made to allow the pus to escape. However, the less surgery done, the more favorable is the prognosis. During the treatment of patients two years of age or more, more bone destruction takes place and the tendency for the acute condition to become chronic is very great.

General supportive measures—chemotherapy, the administration of staphylococcus antitoxin, and management of the local bone disease—are indicated in the treatment of the second type of acute hematogenous osteomyelitis.

Shands and Baker used staphylococcus antitoxin quite extensively and their reports are quite favorable in cases of staphylococcus septicemia with high toxicity. Treating a bone abscess conservatively with sulfonamides alone is using bad judgment. It has been repeatedly shown that definite areas of bone destruction, as shown on roentgenograms, harbor organisms that often cause these areas to flare up with a recurrent attack of acute osteomyelitis.

The author advocates the use of chemotherapy in conjunction with local drainage of the bone abscess by removal of a block of bone and allowing the pus

to escape through an incision in the soft tissues that is kept open with vaseline packs or by the use of the Dakin-Carrell treatment. *George L. Russ, M.D.*

Holt, J. P., and Hodges, F. J.: Significant Skeletal Irregularities of the Hands. *Radiology* 1945 44 23

The authors believe that careful roentgen study of the hands may furnish as valuable information to the radiologist as funduscopic examination does to the ophthalmologist. In reviewing some of the significant abnormalities they lay particular stress upon those carpal, metacarpal, and phalangeal changes which reflect the presence of disease elsewhere in the body.

Endocrine diseases. A good example is the roentgenographic appearance of the hands in acromegaly which indicates the presence of a pituitary eosinophilic adenoma even in the absence of erosion of the sella. Large, broad, spadelike hands with overgrowth of the terminal phalangeal tufts, prominence of bony protuberances along the shafts of the metacarpals and phalanges, and peculiar soap-bubble pattern of distorted trabeculae in the bone ends comprise the changes commonly encountered. In cretinism the delayed epiphyseal ossification and the increased density in the ends of the tubular bones such as one might expect to see in lead poisoning or osteopetrosis, dominate the picture. A knowledge of these changes also helps to differentiate cretinism from mongolian idiocy in which the bone development is relatively normal but the hands may present fairly typical anomalies as, for example, congenital shortening of the middle phalanx of a stubby curved fifth finger. Other abnormalities are the fibrocystic bone lesions of hyperparathyroidism and polyostotic fibrous dysplasia, the peripheral degenerative changes of progeria, and so forth.

Genitalia males. In dysostosis cleidocranialis, in addition to the defective ossification of the bones laid down in membrane, there are characteristic alterations of the hands. The ungual phalanges are short and cone shaped with failure of development of the usual prominent cancellous tufts. The metacarpals, as well as the proximal and middle phalanges, have supernumerary epiphyses which fuse much earlier in life than the normal ones. All epiphyses appear broader than normal. In the hands of the achondroplastic dwarf the second to fifth metacarpals are short, stubby and of nearly equal length. As in the case of the long bones, their ends may be quite bulbous. The phalanges likewise are extremely short and relatively broad. In Morquio's disease the ends of the metacarpals and phalanges are grossly irregular and the carpal bones have a striking crenated appearance. In Hurler's syndrome (gargoylism) the metacarpals are unusually short and broad, the middle phalanges have an arrowhead configuration, and the trabecular pattern is very coarse. Arachnodactylia, or spiderlike fingers, immediately focuses the attention on congenital dislocation of the lenses with congenital heart disease.

Trophic disturbances. These may reflect syringomyelia, leprosy, Raynaud's disease, erythromelalgia, thromboangiitis obliterans, arteriosclerosis, diabetes, scleroderma, and acrosclerosis.

Chronic granulomas. Spina ventosa is a characteristic manifestation of tuberculosis. Osteitis tuberculosa multiplex cystica, as described by Juengling, is another tuberculous manifestation which occasionally is associated with Boeck's sarcoid. Granulomatous lesions produced by pathogenic fungi may also involve the metacarpals and phalanges.

Pulmonia y osteoarthritis pathy. Clubbing of the terminal phalanges with roentgenographic evidence of periosteal proliferation along the shafts of the metacarpals and phalanges is always indicative of pulmonary disease. In fact, its variation in the same individual under the influence of pulmonary therapy carries definite prognostic significance.

Hemopoietic and blood diseases. In this group hemophilia, leucemia, chronic hemolytic anemia, and rarely sickle-cell anemia and chronic hemolytic jaundice may produce diagnostic roentgenographic signs in the hands.

Miscellaneous lesions. Other conditions that may lead to changes in the bones of the hands are osteoarthritis, gout, chondromas, solitary cysts, osteopikilosis, osteopetrosis, melorheostosis, and tuberous sclerosis.

Typical roentgenograms are used to illustrate most of these changes. *T. Livcunia, M.D.*

Sarpyner, M. A.: Congenital Stricture of the Spinal Canal. *J Bone Surg* 1945, 23 70.

The author differentiated 4 congenital strictures of the spinal canal (1) a ringlike constriction of the spinal cord at one or more levels (2) more extensive strictures involving the entire canal (3) a localized stricture and (4) atypical strictures, causing a cleft in the cord in both the cord and dura mater.

Constrictions of the cord in spina bifida occulta were found regularly. The clinical manifestations of a stricture compressing the spinal cord are manifold: enuresis, pains similar to those in lumbago and sciatica, atrophy of the muscles, skin changes similar to vitiligo perforating ulcer, spastic or flaccid paralysis, and various deformities. These patients do not suffer pain because these conditions, like certain spinal tumors which grow slowly exist for a number of years and exert only gradual pressure on the cord. In several patients suffering from enuresis, a lipoidal block was found at the level of the second and third lumbar vertebrae. These patients were not helped by any conservative measures. A definite constriction was found at the level of the second and third lumbar vertebrae at the operation, and upon release of the constriction immediate cure of the enuresis followed. It is also stated that many club feet, several of them of the paralytic type, were cured by laminectomy and release of the congenital stricture of the canal.

X ray films and photographs are presented to illustrate the pre- and postoperative conditions of

the patients. A short outline of the technique of aminectomy is given. In cases of spastic diplegia 5 or 6 vertebrae should be included in the operative field. The stricture must be completely relieved and pulsations must return to the dura below the level of the lesion. In cases of spina bifida it is important not only to remove the tumor but also to relieve the stricture, because if this is not done agenesis of the nerves will continue.

GEORGE I. REISS, M.D.

Kaplan, E. B.: The Surgical and Anatomic Significance of the Mammillary Tubercle of the Last Thoracic Vertebra. *Surgery* 1945 17 78.

Two tables and 8 figures represent in detail a study of the anatomic significance and surgical importance of the mammillary process of the twelfth thoracic vertebra. The mammillary process on this vertebra was found to be large and prominent. This process conceals the upper articular process of the twelfth, and the inferior articular process of the eleventh thoracic vertebra. It represents a good point of localization of the twelfth thoracic vertebra in surgery of the spine. In operations for fusion of the spine involving the eleventh and twelfth thoracic vertebra, the removal of the mammillary process of the twelfth vertebra will allow the proper removal of the cartilage of these facets.

RICHARD J. BENNETT, JR., M.D.

Dandy, W. E.: The Treatment of Spondylolisthesis. *J. Am. Med. Ass.* 1945 137 137.

It is difficult to believe that other discs than the one at the site of the spondylolisthesis are not always affected when the spinal column is thrown out of line by this condition. In this series the concealed discs numbered 33 (75 per cent) as against 11 (25 per cent) that were protruding. This is essentially the same ratio that obtains in discs without spondylolisthesis. Thirteen patients were males and 7 females.

It is the author's impression from his analysis that spondylolisthesis is but an incident in the field of ruptured discs and that, on the whole, while it causes its share of symptoms, it causes less than the contiguous disc or discs. Any treatment that neglected the other discs would accomplish little if any result. Moreover the reason for the development of spondylolisthesis is precisely the same as that for defective discs, i. e. the outward shift in the lateral articulations in the lower three lumbar vertebrae, nearly always most pronounced at the fifth lumbar vertebra. And finally the signs and symptoms of spondylolisthesis are precisely the same as those of defective discs without spondylolisthesis. Only the x-ray appearance makes the differential diagnosis.

If a disc is thoroughly and painstakingly removed with a curet, it cannot recur. This does not mean that every particle of cartilage must be extirpated but it does mean that no large amount can remain. The area of the disc most difficult to remove is dorsal on the contralateral side, and a recurrence with scoliosis on the opposite side will occasionally occur.

In at least 90 per cent, and probably in all of the cases, there are two or three discs (including the one at the site of the spondylolisthesis) which cause the backache and sciatica, and a cure depends on the recognition and treatment of all the affected discs. The disc at the site of the spondylolisthesis causes no more symptoms than the other discs; in fact, on the whole, it causes even less.

A cure results when the discs are completely removed. The end result of removal of the discs is fusion of the opposing vertebrae and, therefore, stabilization of the spine. This obviates the necessity of fusion by means of bone grafts to the spine. Statistics on the results are presented.

Spinal fusion by grafting is never indicated either for spondylolisthesis or for defective intervertebral discs. Its continued use means that the discs have been improperly recognized or treated or both.

ROBERT P. MONTGOMERY, M.D.

Green, W. T.: Slipping of the Upper Femoral Epiphysis: Diagnostic and Therapeutic Considerations. *Arch. Surg.*, 1945, 50 19.

The author reports 26 cases of slipping of the upper femoral epiphysis or epiphysiolysis. The total number of hips involved in these cases totaled 36. They represented all slipped femoral epiphyses seen by the writer in thirteen and one half years.

The mechanism is that of an insidious inherent weakness developed between the head and neck of the femur at the metaphysis which results in a downward displacement of the head and an upward and anterior displacement of the neck. Derangement varies from an undetectable degree to a complete epiphysal separation.

The etiology is obscure. It affects both sexes between the ages of ten and fifteen years. Obese children are more susceptible. Other factors are trauma, endocrine disturbances, periosteal insufficiencies, and vascular abnormalities about the femoral neck.

The clinical picture is one of an obese child who acquires an antalgic hip limp, pain in the homolateral knee or hip, limitation of internal rotation, flexion and abduction, hyperextension of the involved hip and muscular spasm.

Röntgen examination discloses rarefaction of the neck adjacent to the epiphysal line and (early) minimal displacement of the femoral head. Irregular callus may be noted if the slipping is of long standing.

The author employed 5 different forms of treatment among the 36 hips.

1 Closed reduction with spica fixation. Three cases were treated with satisfactory results.

2 Traction spica method without manipulation. Eighteen hips in 13 patients were restored to excellent function. While there was an average shortening of 1 cm. in the treated hips a normal coefficient of motion of 98.5 was attained in the majority of cases.

3 Skeletal fixation *in situ* (without arthrotomy) for those hips with minimal displacement. Five hips were so treated by means of a modified Smith-Peter

seen. While the results were classified as good, there was a diminished coefficient of motion, i.e., from 80.5 to 84.5. One of the 5 patients suffered further displacement of the epiphysis following operation from excessive growth of the neck.

4. Open reduction with skeletal fixation was reserved for those hips with pronounced derangement. The results in 3 of the 4 hips treated in this manner were classified as poor. In the other 3 cases excellent functional results were obtained after modification of the operative procedure.

5. Miscellaneous methods, including traction, non-weight-bearing brace, and crutches were used in the remainder of the cases.

Operation includes preservation of the periosteum about the neck, meticulous care of the inferior cervical vessel (reticula of Weitbrecht), removal of the soft osteoid, restoration of normal alignment, and firm fixation. The author prefers the Moore type of nail. Arthrolysis is accomplished through a lateral exposure.

SAMUEL L. GOVERMAN, M.D.

Cox, F. J.: Traumatic Osteochondritis of the Patella. *Surgery* 1945 17 93.

When a direct blow to the patella is received the patella is driven against the adjacent femoral condyle and a greater or lesser degree of compressive force is exerted upon the subchondral bone. This causes the development of areas of necrosis in the subchondral bone of the patella and femoral condyles which can be considered in almost the same light as a fracture. If the initiating trauma is mild and the amount of damage to the subchondral bone is minimal spontaneous absorption and repair of the involved bone may occur. If, however, the area of necrosis in the subchondral bone is more extensive, the area of involved bone is walled off and becomes a true sequestrum. Immediately gross interference with the nutrition to the overlying articular cartilage layer develops, and consequent degenerative changes in that cartilage begin to appear. When these changes persist for a period of time, thinning of the articular cartilage of the patella, irregularities in contour and fissures may occur. As a later manifestation the synovium of the knee joint becomes irritated. In response to this irritation hypertrophy of the synovium and a chronic effusion result. Should the lesion remain untreated for a period of years, progressive arthritic changes in the knee joint will be found. The lesion is certainly not uncommon.

The author presents 6 examples of this condition that have come to his attention.

In all cases except 1 a direct injury to the patellar region was established which forced this bone against the anterosuperior surface of the medial femoral condyle. This resulted in immediate temporary disability caused by local swelling and pain upon flexion or extension of the knee joint.

The acute symptoms referable to the knee joint subsided for several weeks or months. With the passage of time there appeared a low grade chronic effusion which fluctuated in degree with the extent

and character of exercise indulged in by the patient. Definite vague symptoms of discomfort persisted within the knee joint and vague pain was felt on its anterior aspect. This sometimes was made worse by exerting strain upon the flexed knee through the quadriceps apparatus as when kneeling or squatting. All of the patients complained of occasional symptoms of locking, or "catching." The condition was chronic.

The following gross pathological changes were noted at operation: (1) softening irregularity in contour and fissure formation in the articular cartilage of the patella. (2) yellowish discoloration of the articular cartilage in the areas of involvement. (3) similar changes in the articular cartilage of the femoral condyle on its anteromedial aspect. (4) thickening, hyperemia, and villous degeneration of the synovium, usually confined to the suprapatellar pouch region and the anterior compartment of the knee joint. (5) increase in the amount of the joint fluid, usually clear yellow in color with a normal cell count, or slight increase in polymorphonuclear cells and (6) pannus formation at the edges of the articular cartilage of the patella and femoral condyles.

In the author's opinion the true pathological change is to be found in the underlying cancellous bone, and the change in the articular cartilage is an entirely secondary one. All cases in the literature emphasize the cartilaginous changes.

All of the 6 patients treated by excision of the patella, with the synovium and degenerated femoral cartilage left undisturbed made complete recoveries, with disappearance of the synovitis and effusion in every instance. Some other factor may well be the cause of the late development of arthritic change. Removal of the involved cartilage alone has caused subsidence of the synovitis and secondary joint changes. Patellarplasty has given good results, although apparently not quite as good as patellectomy. The author is not completely convinced that removal of the patella in the human being will lead to arthritic changes in later life. Although there is no definite proof at this time it is believed that the more severe and permanent changes resulting from an osteoarthritis have been obviated in this group of patients by removal of the patella. The lesson, as described is rare by admission, but perhaps not so rare as it might seem at first glance. If the under surface of the patella were routinely inspected in every exploratory operation for internal derangement of the knee joint, probably more cases would be encountered.

ROBERT P. MONTGOMERY, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Jones, L.: Complete Rupture of the Supraspinatus Tendon: A Simplified Operative Repair. *Arch. Surg.* 1944, 49 390.

This article is based upon a series of 51 cases of painful shoulder among which were found 3 cases of complete rupture of the supraspinatus tendon. The

lines of force which pass through the musculotendinous cuff are present in aggravated form at the circular portion of the supraspinatus tendon just above the point of final attachment to the horizontal line of the greater tuberosity of the humerus. When rupture once occurs in this weakened area there is a retraction of the edges due to the pull of the force from four directions—superior inferior anterior and posterior. Even the dependency of the arm helps to keep the rent open. Nature attempts to heal this defect by scar tissue often associated with a calcium deposit. A low grade inflammation is often present.

Three cases of complete rupture of the supraspinatus tendon were repaired by a new operative procedure. On the basis of cases in which the head of the humerus has been discarded and the capsule has been reattached to the upper end of the shaft by means of bony grooves, a stable shoulder results. When these grooves are arranged in a physiological pattern the stability is accompanied by nearly complete functional recovery. The short rotator or capsular muscles are considered in three groups. They are (1) the subscapularis (2) the supraspinatus and (3) the infraspinatus and teres minor muscle. These fuse with the capsule of the shoulder joint before a final bony insertion to form a conjoined tendon. The supraspinatus inserts into the transverse line of the greater tuberosity. The infraspinatus-teres minor group inserts into the posterior descending line. The subscapularis group inserts into the lesser tuberosity of the humerus and the anterior border of the bicipital groove. This group of three muscles working together constitutes an antagonist for the deltoid muscle. The combined weight of these three is approximately the same as that of the deltoid muscle. The complete loss of abduction cannot be due to the loss of the supraspinatus muscle alone. These three powerful muscles pull not only against the bony insertions but against each other through their central junction in the conjoined tendon. The presence of a central supraspinatus-tendon rupture definitely produces inaction of the neighboring muscles, specifically the subscapularis in front and the infraspinatus-teres minor muscle in back. From these anatomic facts it seemed reasonable that a flap from the contiguous upper portion of the infraspinatus muscle could be transplanted as a substitute for the ruptured and retracted tendon of the supraspinatus muscle. In a large defect two flaps were used one from the infraspinatus and the other from the subscapularis.

The first patient was a female, age twenty-six with pain in the left shoulder of seven years duration. There was a definite injury followed by pain which persisted. The patient had been treated conservatively for a subacromial bursitis. Diagnosis of rupture of the supraspinatus tendon was made. Manipulation of the arm was necessary during operation to facilitate fixation and closure. A Cubbins acromioclavicular incision was used. The deltoid muscle was elevated and incised close to its attach-

ments. The anterior two-thirds of the deltoid muscle were reflected downward as a flap. A complete rupture of the supraspinatus tendon was found. A 1 inch transverse groove was made on the lateral surface of the humerus just below the transverse line of the greater tuberosity. Two drilled holes were made at each end and at right angles to the end of the groove. The infraspinatus muscle was fixed into the groove by means of silk suture. The edges of the transplant were sutured to neighboring muscles to re-establish continuity. An abduction splint was used with the arm maintained at 60 degrees. The patient had complete return of function after four months.

The second patient was a male, age seventy who after injury was unable to abduct his arm. He was given physical therapy. During operation, and after the deltoid muscle had been reflected, a tear was visualized which involved the three groups of muscles. It is better described as a complete avulsion. Here two bony grooves were made one transversely and one vertically and it was necessary to supplement them with a piece of fascia. The subscapularis was sutured into the anterior groove, and the infraspinatus-teres minor and supraspinatus were sutured into the vertical groove. Closure was made by means of a fascial continuous running suture. The edges of the flap were sutured to each other and continuity was re-established. The patient's arm was abducted 45 degrees on a splint and no movement was allowed for six weeks. Seventeen months later the patient had a completely painless shoulder with abduction to 60 degrees.

The third case was that of a male age sixty who suffered severe injury. Avulsion of the upper capsular segment was found to be quite extensive. A very similar operative procedure to that used for the second patient was employed. Eleven months after injury the patient was able to abduct his arm to 90 degrees.

RICHARD J. BENNETT, JR., M.D.

Aitken A. P.: Stenosing Tendovaginitis at the Radial Styloid Process (De Quervain's Disease). *N. England J. M.*, 1945 332 105.

De Quervain's disease is caused by a thickening of the tendon sheath covering the abductor pollicis longus and extensor pollicis brevis as they pass over the radial styloid process. This disease is seen in women much more frequently than in men. It may be present for several months and then become acute, following a trauma. It is rarely seen in persons over twenty five years of age. It often occurs in cooks, nurses, and housewives. Finkelstein described a test which is pathognomonic for this condition.

The thumb is placed in the palm of the hand and the forefingers are flexed tightly over it. Ulnar deviation of the hand then causes severe pain over the radial styloid process, but radial deviation causes no discomfort.

Fractures of the carpal navicular have to be differentiated from De Quervain's disease. In fractures

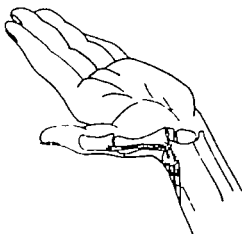


Fig. Diagram showing the location of the fibrous sheath at the radial styloid and the divergence of the short extensor and long abductor on abduction or extension of the wrist.

of the navicular there is pain in the anatomical snuffbox, and motion and movements of the thumb are not as painful as in De Quervain's disease.

The treatment of choice is surgery. An incision about 4 cm. in length is made over the tendons at the level of the radial styloid process. The tendon sheath is opened, fibrous thickened tissues, as well as adhesions, are excised and only the skin is sutured. Motions are started the day following the operation. No recurrences have been seen. Keloids have developed in the incisions because of encouraged early motion following the operation.

GEORGE L. REISS, M.D.

Smith Petersen, M. N., Larson, C. B., and Aufranc, O. E.: Osteotomy of the Spine for Correction of Flexion Deformity in Rheumatoid Arthritis. *J Bone Surg* 1945 8

In osteotomy of the spine the operative procedure is confined to the laminae and articular facets and does not involve the vertebral bodies.

Recumbency in the position of minimum pain commonly results in a flexion deformity of the spine sufficiently marked to interfere with the function of the lower extremities in standing and walking and to make the sitting position one of strain and discomfort.

Manipulation, followed by support, will improve many of these patients but it will not be of benefit after bony ankylosis of the articular facets and calcification of the longitudinal ligaments have occurred. Patients with ankylosis of both hips not infrequently present this latter extreme condition of the spine.

After arthroplasties the flexion deformity of the spine interferes to such an extent with function of the lower extremities that the problem of correction becomes most important. Analyzing the obstacles to correction, the authors came to the conclusion

that the ankylosed facets surrounded by overgrowth of bone offered more resistance than any of the other spinal structures.

Any surgical procedure for correction of the flexion deformity must, therefore be aimed at the facets, articular processes and adjacent laminae, osteotomy of these structures, with excision of sufficient bone should allow corrective leverage to be transmitted to the intervertebral discs and longitudinal ligaments, and overcome whatever resistance they may present.

Surgical intervention in rheumatoid arthritis should be undertaken early before secondary deformities develop.

The lumbar region is more favorable than the thoracic since the latter commonly presents ankylosed costovertebral joints which make correction difficult, if not impossible. Thoracic osteotomy was done in only 1 case; it resulted in subjective improvement, but there was no objective evidence of it.

Selection of the lumbar level or levels at which the osteotomy is to be performed depends on the roentgenographic findings, the less marked the ossification the better the chance of correction.

A description of the operative technique with special emphasis upon aspects that are likely to cause technical difficulties is presented.

In the postoperative care a plaster shell is applied and kept on for from four to six weeks; this is followed by a plaster jacket or back brace which is to be worn continuously for a year or longer. Since complete correction is never obtained it is important to guard against recurring deformity by having the patient wear the brace during part of the day for two or three years postoperatively. It is hardly necessary to emphasize the importance of exercises for the control of posture as well as for the maintenance of chest expansion.

The author states that osteotomy of the spine, performed in a series of 6 cases, has yielded satisfactory results.

ROBERT P. MORRISON, M.D.

Boerworth, D. M.: Clothespin Graft of the Spine for Spondylolisthesis and Laminar Defects. *Am. J. Surg* 1945, 67 6

The clothespin graft consists of a bone graft with the ends notched out to receive spinous processes at either end of the fusion area. During placement the patient is in flexion with the spinous processes separated. Following operation the patient is extended and the graft is maintained firmly in position.

The intervertebral laminae of the graft area were definitely enlarged and apparently reduction of the vertebral body in spondylolisthesis was secured. Decompression of the nerve roots and immediate relief of the compression pain were also obtained. The first grafts were of tibial bone; later massive iliac bone grafts were used. These single fusions were reinforced with separate iliac strips. Forty-seven cases were operated upon with 1 mortality. Fracture

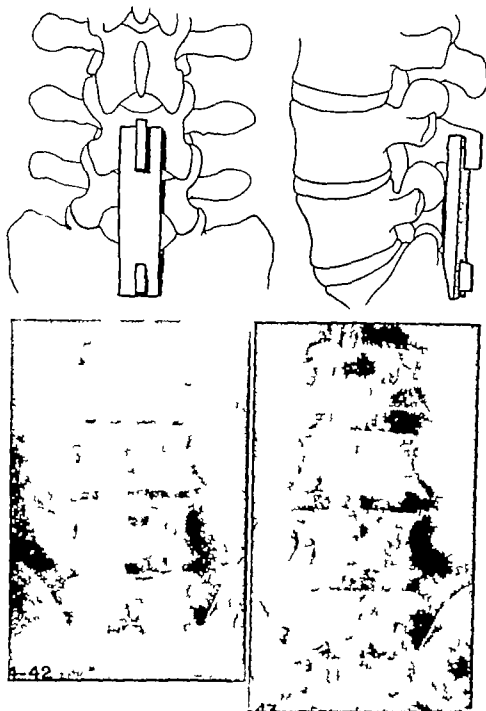


Fig. 1. Double clothespin graft has great strength, is firmly maintained in position when applied with the spine in flexion and then extended to normal, and provides a distracting force to separate intervertebral spaces as well as secure fusion. Note the opening of the third lumbar intervertebral space and separation of left fifth lumbar and first sacral articular facet caused by long clothespin graft as shown in roentgenograms. (Courtesy of American Journal of Surgery)

of the body of the graft has not occurred but there were postoperative infections. Two grafts were removed for aseptic necrosis; the cultures were negative and primary healing followed removal. Spontaneous fracture of the tibia at the site of osteotomy occurred in 4 instances. The spinous-process abutment on the sacrum was dislodged by graft compression

in 3 instances postoperatively. Several complications accompanied these procedures. Hospitalization varied from twelve days to four months. Among the uncomplicated cases the average time of hospitalization was three weeks. Plaster jackets were applied two and one half weeks postoperatively and these were worn for five months.

Several variations of this clothespin graft have been used. There were numerous variations of the area grafted. Several conditions were listed for which the operation was performed. Fifty-five patients were operated upon before January 1943. Clinically there was solid spinal fusion in 49 cases (89 per cent) there were 4 clinical failures. It is believed the only accurate method of determining solid spinal fusion is by flexion and extension x rays. Thirty-three of 41 cases have been checked with these, most of the x-rays showed the fusions to be completely solid. Among 11 instances of spondylolisthesis, 8 fusions were proved to be solid by x ray studies. Among these there was 1 failure. Clinical relief was obtained in all of the patients except 4 who were partially relieved and 4 others who were unrelieved. These failures are analyzed.

RICHARD J. BROOKETT JR., M.D.

Thompson, T. C., and Alldredge, R. H.: Amputations; Surgery and Plastic Repair. *J Bone Surg* 1944, 26 639.

The guillotine operation has many advantages, especially under wartime conditions.

1. It is a simple débridement of the end of the extremity easily accomplished under adverse conditions.

2. It is rarely followed by spreading infection in bones or soft parts.

3. It saves more extremity than any other method.

4. If skin traction is soon applied and maintained until the patient arrives at the Amputation Center preparation of a satisfactory stump is simple.

Its advantages are

1. No devitalized tissue is left in which infection will persist or spread.

2. The raw surface exposed is not large, and has a good blood supply.

3. If the skin traction is constant the scar formation at the end tends to pull the soft tissues over the end of the bone and results in a firm, smooth, conical stump.

4. Repair necessitates only the excision of scar tissue and perhaps a small tip of bone, and normal skin and subcutaneous tissue are easily fashioned and closed without tension.

5. These stumps are as good as those obtained by primary amputations at sites of election and can be quickly fitted with a prosthesis. When revision of the stump is necessary it heals promptly with rapid shrinkage of the stump.

6. The frequent complications of primary or early secondary closure are avoided.

The authors advise against the use of pin fixation above the site of a severe compound fracture if an attempt is to be made to save the limb, as amputation has eventually been necessary at the level of the upper pin. Otherwise amputation may have been at the site of fracture.

The time for revision or reamputation of a stump depends upon various factors. If the stump is short, skin traction should be maintained as long as healing

continues. The type of dressings should depend upon the type of organisms present. Sulfonamides are used preoperatively and postoperatively, and the administration of penicillin twenty-four hours before and fourteen days after operation permits excision of the scar and granulation tissue and even of sequestra for skin closure. When the bacteria are penicillin-resistant, wound infection should be controlled after sequestrectomy before closure is attempted.

In order to secure smooth skin margins without tension, the skin flaps must be undermined a considerable distance. Deep stay sutures are unnecessary as they often produce depressed transverse scars across the main scar. A rubber tissue drain is inserted at each end from one to three days. Post-operative skin traction is used when tension on the suture line from postoperative swelling is suspected.

Plastic repair should be performed on most guillotine stumps in order to provide the best possible stump.

ROBERT S. REICK, M.D.

Peterson, L. T.: The Army Amputation Program. *J Bone Surg* 1944, 26 635.

In May 1943 the Surgeon General directed the establishment of 5 Amputation Centers in various sections of the country for the purpose of co-ordinating and standardizing the treatment and fitting of amputees.

Early in the present war three difficulties were encountered in the treatment of amputations.

1. Primary closure is definitely contraindicated in military surgery as it is likely to cause cellulitis, osteomyelitis, or gas gangrene which may endanger the patient's life and may necessitate additional sacrifice of the extremity.

2. In some patients the guillotine operation had been performed higher than necessary either through or above the level of election for a finished stump.

3. Early and continuous skin traction is imperative in open amputation technique, as failure of adequate traction results in the retraction of the soft tissue. A skin graft is not an acceptable substitute as it does not ordinarily withstand the pressure of a prosthesis.

As soon as the stump has been properly treated by surgery and physical therapy it is fitted with an artificial limb. The Amputation Centers have completely equipped shops. On the lower extremity the amputees are fitted with a provisional prosthesis which may be refitted or adjusted later as required. On the upper extremity the prosthesis requires less change. The patient is fitted with the particular features which best suit his needs.

The statistics of this war indicate that 25 per cent of the total amputations resulted from training accidents, accidents not related to military activity, vascular diseases, and tumors. One amputee in 30 lost 2 extremities less than 1 in 300 was amputated at the hip joint, while amputations below the knee and elbow predominate. On admission, 361 patients (21.6 per cent) were ready for prostheses, while 1,399

(78.4 per cent) required further surgery before proper fitting was possible.

In addition the amputee with a prosthesis for the leg is taught how to walk by the physical therapist, while the amputee with a prosthesis for the arm is trained in the use of the attachments to this prosthesis.

RUDOLPH S. RICH, M.D.

FRACTURES AND DISLOCATIONS

Murray G.: Longitudinal Wires in Bones in the Treatment of Fractures and Dislocations. *Am. J. Surg.* 1945 67 156.

Longitudinal wires in bones have provided excellent fixation of certain selected fractures and in particular those fractures in which it has been difficult to obtain satisfactory fixation by external splinting either with or without skeletal pins.

In fractures of the clavicle, scapula, both bones of the forearm, some cases of fracture of the humerus and long bones of the hands and feet, it provides a method by which greatly improved results in these fractures can be expected. Acromio and coracoclavicular dislocations are easily controlled by this method. Naturally as in all procedures in which it is necessary to make an opening in the skin the most rigid aseptic surgical technique must be observed. In the author's experience there has been one infection in which it was necessary to remove the wire because of the infection.

In the humerus the wire is passed through the greater tuberosity and vertically down the shaft the wire is placed in an extra-articular position. Passed in this way it gives excellent control of fractures of

the high surgical neck or shaft. With such a wire in position the arm has been carried in a sling only and excellent union in a good position has resulted. In the forearm with fractures of both bones, the subcutaneous olecranon provides a very easy approach through which to pass the wire through the proximal and into the distal fragment. In the radius the subcutaneous styloid process offers an easy and extra-articular approach through which the wire can be passed through the distal and into the proximal fragment. If after reduction and fixation of the ulna with the wire the radius can be reduced it also is held by a wire. If however the fragments are so engaged that closed reduction is impossible a short incision over each bone should be made and accurate reduction obtained. The wires then passed as described, provide excellent fixation which is quite easy to apply. To date all such fractures have been fixed in plaster casts until evidence of union has taken place. In the metacarpals and phalanges when reduction has been obtained the wire can be passed in the case of the metacarpal it is passed through the distal articular end and across the fracture line into the proximal fragment, with the proximal phalanx flexed to an angle of about 45 degrees. If the fracture is at the neck or near the head of the metacarpal the wire is best passed through the distal articular end of the proximal phalanx through its medullary cavity across the metacarpophalangeal joint through the distal fragment, and well into the proximal fragment. In fractures of the phalanges after reduction the wire is passed either through the distal articular end of the affected phalanx or through the tip of the finger and across the interphalangeal



Fig. 1. Comminuted fracture of both bones of the forearm satisfactory result by wire fixation. (Courtesy of American Journal of Surgery)

joint, if necessary. In none of these fractures has there been evidence of any ill effect in the way of discomfort or disability as a result of the fine wire traversing the articular cartilages.

This form of fixation is the most satisfactory in fractures of the clavicle. In dislocations of the acromioclavicular joint, fixation by two or more wires gives a most satisfactory result with no permanent deformity.

With acromioclavicular and wide coracoclavicular separation, fixation of the acromioclavicular joint by wires also provides a very easy and effective method of allowing repair of the coracoclavicular ligaments with subsequent excellent stability and function of the shoulder girdle.

Longitudinal wires also provide an easy and excellent method of fixation of internal and external malleolar fractures at the ankle when closed methods of reduction are not satisfactory.

Use of wires in a similar way offers excellent fixation in arthrodesis of interphalangeal or metacarpophalangeal joints in the hand or foot.

In Cant's subtrochanteric osteotomy to correct an adduction deformity, the lower fragment tends to be displaced medially when the femur is divided across. The procedure is greatly facilitated and the fixation is adequate when a longitudinal wire is passed through the tip of the great trochanter and down the shaft of the femur.

A series of illustrative cases is shown by x rays that demonstrate the use of the wires and the end results obtained. This report is based upon 154 patients treated with longitudinally placed wires. None of the wires has drifted out of the field.

The presence of the wire across the fracture line has not impeded the rate of union of the fracture and there were no nonunions in this series. On the contrary in the majority of cases these fractures united in a shorter time than ordinarily would have been expected.

Longitudinal wires in bones have provided excellent fixation of certain selected fractures and in particular those fractures in which it has been difficult to obtain satisfactory fixation by external splinting either with or without skeletal pins.

There has been no evidence that a small or medium-sized Kirchner wire which traverses articular cartilage produces any deleterious effect on the joint. ROBERT P. MONTGOMERY, M.D.

Boonin, J. G.: Sacral Fractures and Injuries to the Cauda Equina. *J Bone Surg* 1945, 23 115.

The lateral portions of the sacrum are weakened by the first and second sacral foramina. Most of the fractures, therefore, occur in this portion of the body and sometimes spread from this portion to other areas of the pelvis, for example, to the innominate bones. Most of the sacral fractures are caused secondarily to pelvic injuries and by violence applied to one side of the body or one leg.

The sacral fracture might be caused by the following conditions

1. By a rotation injury. The hyperextended lower leg is pushed backward. The affected innominate bone is rotated in a horizontal axis which causes the fracture line to run through the first and second sacral foramina. This injury very often is associated with a separation of the pubic symphysis or a fracture of the ischiopubic ramus.

2. By leverage. The violence is transmitted through the abducted lower extremity. This usually occurs in run-over accidents.

3. By shearing force. One-half of the pelvis is driven directly backward by an impact against the knee of the patient in sitting position. In 45 per cent of all pelvic fractures the sacrum is involved. The sacrum is described in detail as it appears on routine anterior and posterior roentgenograms and certain important landmarks are pointed out.

The neurological signs are caused by compression of the first and/or second sacral nerve roots. These findings correspond with other conditions involving these nerve roots. Injury to these nerve roots may be caused by pressure of small fragments of bone, by surrounding hemorrhage, stretching, or by contraction of fibrous tissue or callus.

The most characteristic feature of sacral fracture extending through the first and/or second foramen is the distribution of muscle paresis. Paresis of the buttock, hamstrings, and calf muscles characterize the lesion, according to the author. Marked paralysis of the biceps femoris was observed in all cases and is probably the most distinctive sign in this condition. The loss of ankle reflex, combined with fibrillation of the calf muscles, is very often seen. In spite of the disagreement among authorities as to the different areas of the dermatomes supplied by the first and second sacral nerves, the following skin areas usually show sensory changes: a small area of hypesthesia to light touch and pinprick on the medial aspect of the left buttock with a surrounding area of hyperalgesia, hypesthesia or anesthesia of the back of the lower half of the leg, the outer side of the foot, and part of the sole. Similar findings are found in herniated nucleus pulposus. In this condition, however usually one single nerve root is affected.

The pain pattern of these two conditions can be considered as a differential diagnostic point. Pain in herniated nucleus pulposus which arises from tension on the nerve is more or less of a constant nature. The pain in sacral fractures is severe at the onset of the injury but rapidly subsides. This is due to the fact that in sacral injuries the nerve usually is severed. Bladder and bowel disturbances are infrequent because sacral fractures are usually unilateral.

The treatment consists of a counterbalanced sling around the pelvis of the patient with traction on the lower extremity and physical therapeutic measures. In the average type of sacral fractures the prognosis is good. There is usually complete recovery and only occasionally some weakness in the affected leg with slight permanent muscle wasting.

Case reports roentgenograms, and photographs of 5 patients with sacral fractures combined with pelvic fractures are presented
 GEORGE I. REISS, M.D.

Boucher, D. W.: Internal Fixation of Fractures of the Neck of the Femur. *Consil. M. Ass. J.*, 1945
 32-33

When severe pain persists after an accident involving the fracture of the neck of the femur internal fixation by nailing should be carried out as soon as possible. Preoperative extension has not been used and the author believes that fractures forty-eight hours old reduce as easily as those of a few hours duration. In handling these patients the anesthetic is usually nitrous oxide and oxygen given by spinal or local infiltration. When both surgeon and radiologist understand each other's abilities and problems the operative time is decreased.

The procedure consists primarily of anesthetizing the patient in the recumbent position, and Leadbeater's maneuver of reduction is carried out. After reduction the thigh is in abduction, hyperextension and internal rotation. The nailing is carried out by the extra articular technique.

None of the cases showed any sepsis and the wounds healed without discharge.

The methods suggested by Hey Groves and Watson Jones are followed. An incision is made on the lateral thigh in the subtrochanteric region. Guide wire is inserted and the nail driven in. The guide wire is then removed and anteroposterior and lateral x-rays are taken. With the position satisfactory, the incision is closed.

After closure, various movements of the hip joint are carried out by the surgeon and act as a guide to the thoroughness of the operative procedure. In bed the limb is supported with a soft pillow. Full leg exercises are begun twenty-four hours after operation. If the patient's condition permits he is allowed up in a chair on the fourth day bearing no weight on the leg. Patients are allowed up on crutches after the third week until the ninth week when they may bear weight on the injured leg. After that, the crutches are discarded as soon as the patient is able to get along without them.

Vascular necrosis of the head with associated osteoarthritis, absorption of the neck, and poor nail ing are complications which have occurred. An excellent result means painless movement without the slightest deformity or limp. No nails have been extracted except in the one case of absorption of the neck.

Forty-three case reports are abstracted. 16 roentgenograms are included. Sixteen and two-tenths per cent were subcapital fractures. 47.8 per cent were transcervical and basilar fractures; either intertrochanteric or pertrochanteric, occurred in 41.8 per cent. Fractures in females accounted for 83.2 per cent of the total. The end results were listed as good 72.3 per cent, fair 8.3 per cent and poor 8.3 per cent. 10.6 per cent of the patients died.

RICHARD J. BROWETT, JR., M.D.

Stanek, W. F.: Internal Derangements and Fractures Involving the Knee. Results of 156 Consecutive Arthroplasties Performed at a Station Hospital. *J. Bone Surg.* 1945 28-86

Injury to the knee, recent or old, constitutes one of the major problems of orthopedic surgery in the Army. Some surgeons assert that few soldiers operated upon for internal derangements return to full duty and it has been difficult to account for this. The author has therefore reviewed 156 cases of arthroplasty. These cases were divided into 6 classes in order that they might be more readily evaluated. The first 75 were originally tabulated in January, 1943 and include the patients operated upon from April through December, 1942 (Group 1). On the basis of the results obtained, certain changes were then made in the choice of cases to be subjected to operation. The second series of patients were operated on between January and October, 1943 (Group 2). The more interesting and unusual cases are briefly described in the original article.

In every case exploration of the anterior chamber of the knee was continued until the different pathological changes were located or a thorough examination was completed. Negative as well as positive findings were recorded on the operative sheets, a fact of considerable importance in the later evaluation of several of the cases. When a meniscus was removed as much of it was taken out as could be obtained through an anterior incision. When it was thought that the remaining portion might cause later difficulty a Henderson incision was used to obtain the remainder of the meniscus. In simple cases of injury to the meniscus, sheet wadding and muslin dressings were applied, quadriceps-setting exercises were started on the first postoperative day and the man was allowed to be up without crutches as soon as he could raise his leg unassisted from the bed. Frequently on the second or third postoperative day. No attempt was made to repair torn cruciate ligaments. Of the 156 cases, 103 showed injury only to the menisci, ligaments, or fat pad. Eighty-six torn medial menisci and 15 torn lateral menisci were removed. Two cases showed tearing of both menisci. Fifty-four bucket handle, 20 anterior, 10 posterior and 3 minimal tears (loose anterior attachments) are recorded.

Of this group of patients, 97 returned to some type of duty. In 24 cases disorders of the bone and articular cartilage were shown. Of 9 patients with osteochondritis dissecans, 8 are believed to be on duty while 11 with chondromalacia of the patella, 8 are probably still in service. Only 5 patients with severe arthritis were operated upon, and none of these are believed to be in the Army at present. Nine patients with recent or old fractures involving the patella, tibial spine, or tibial plateau were operated upon. Five of these have been discharged for disability. The last man of the group was discharged because of an ankle disability. Of the remaining patients in the series, those operated upon primarily for diagnosis have shown poor results. The

final diagnosis in most cases being psychoneurosis. Three unusual cases were found, and were described in detail

EMIL C. ROSENTHAL, M.D.

ORTHOPEDICS IN GENERAL

Thomas, A.: Anatomic and Physiological Considerations in the Alignment and Fitting of Amputation Protheses for the Lower Extremity *J Bone Surg* 1944, 26 645.

The efficiency and ease with which the amputee walks with his prosthesis depends upon the alignment and fit of the prosthesis, the site of amputation, the length and condition of the stump, muscle strength, mobility of the adjacent joints, and the mental attitude, skill, and aptitude of the amputee.

In the below-the-knee amputation, there is remarkably little disturbance of gait, because of a normally functioning quadriceps. The artificial foot gives adequate function through rubber cushions provided for by elastic pressure.

For amputations above the knee, walking depends mainly upon the success and control of the artificial knee joint. Elastic straps or inner springs are not essential to locomotion as the gait is similar to that of a person with a paralyzed quadriceps. The thigh is extended by the *gluteus maximus* and the absent calf muscles are substituted by placing the foot in slight plantar flexion. The stability of the knee joint is increased by placing of the axis of the knee joint posterior to the knee center.

The head and neck of the femur forms an angle of 125 degrees with the shaft, the longitudinal axis of which in the frontal plane is directed obliquely downward and inward. In the sagittal plane the femur curves slightly anteriorly. The hip joint of the prosthesis must be well anterior to the greater trochanter to coincide with the true axis in flexion and extension.

In order to compensate for the gliding mechanism of the artificial knee joint this is achieved by placing the knee bolt or side joint posterior to the knee center.

Function of the foot of the prosthesis is obtained by dorsal and plantar flexion only, and motion of the

metatarsophalangeal joints must be provided for and must correspond to the axis of the normal foot. It is important to provide toeing out of the artificial foot equal to the rotation of the normal foot in order to prevent rotation of the prosthesis on the stump which would cause abnormal friction and pressure. The opposite extremity must be matched closely in order to obtain as near a normal gait as possible.

The socket of the prosthesis for thigh amputations must be accurately shaped and fitted in order to bear weight comfortably and not interfere with the circulation of the stump. The socket is roughly triangular in shape and is constructed to bear weight on the ischial tuberosity, the lateral surface of the thigh, and greater trochanter. There is no stump weight bearing except in the case of amputations at or just above the knee.

For amputation below the knee, the socket must be so constructed that it will accurately fit the regular surface of the weight-bearing areas below the knee: the tibial condyles, the tibial tubercle, and the head of the fibula. The prosthesis must not cause any pressure in the popliteal space, as this would interfere with the circulation and cause edema. The socket should fit snugly and afford up-and-down motion. The posterior border of the socket should extend just as high as the anterior in order to avoid bulging of the soft tissues of the popliteal space. The side joints at the knee should be set posterior to the lateral knee center.

Suspension from the shoulders by means of a harness is still in common use, but pelvic suspension is becoming more popular as it affords a more normal and less fatiguing gait. It is attached to the prosthesis by means of a joint at the hip and should be well anterior to the greater trochanter to coincide with the true axis of the joint.

The lengths of the lower and upper extremity prostheses should closely approximate the normal leg, especially when pelvic suspension is used.

In short thigh stumps in aged or debilitated persons, the shoulder suspension is necessary and the prosthesis should be from $\frac{1}{4}$ to 1 inch shorter.

RUDOLPH S. REICH, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Rogers, L.: Carotid Ligation for Intracranial Aneurysm. *Brit. J. Surg.* 1944, 32: 309

A healthy man aged twenty two while driving a car had a sudden severe headache which necessitated his stopping and handing the steering wheel over to a passenger. For a fortnight previously he had noticed occasional twitching of his right eye. On waking on the morning after his attack of severe headache, he was unable to open the eye voluntarily. When the upper lid was forcibly raised the vision was found to be blurred. The condition gradually cleared up but five years later he began suffering from attacks of pain behind the right eye which caused a total disability.

He was a well built man with ptosis and a dilated inactive pupil on the right side. Movements of the eyeball were defective. The blood pressure was 210/100. X rays showed some calcification which was regarded as occurring in an aneurysm of the right internal carotid artery. The cerebrospinal fluid pressure was 180 mm. its protein content well below normal, and the Wasserman reaction negative. An electroencephalogram revealed nothing abnormal in any area either when resting or during overbreathing.

From April 5 until April 28, 1944, digital compression of the right common carotid artery was performed, at first for five minutes, later as long as twenty minutes each day. On April 29 the right common carotid artery was exposed under novocain infiltration and temporarily occluded by a piece of tape surrounded by four waxed silken threads tied over it in a half hitch which was held in the beak of a curved hemostat. The systolic blood pressure was now 190 and remained so throughout the operation. Dynamometer readings were taken every three minutes from both hands over a period of an hour and a half and at intervals during this time electroencephalograms were also obtained and reported upon as follows:

During occlusion of the right common carotid the right hemisphere showed slightly more prominent normal rhythms than the left. These were never outside the physiological range and towards the end of the period (1 hour 20 minutes after occlusion) the asymmetry was less marked than at first. These observations suggest that the carotid occlusion did not result in any significant arterial anoxia.

As neither the electroencephalogram nor the dynamometer readings gave any indication of serious impairment of cerebral function the common carotid artery was secured in two places by silk ligatures and divided between these. A striking phenomenon was the extent of the retraction of the divided ends of the vessel, so that they were separated by at least an inch.

The pain left the ptosis lessened, and the movements of the eyeball improved and with them the vision. There has been no hemiplegia. An electroencephalogram three weeks after operation showed all rhythms within normal frequency which confirmed the belief that the carotid occlusion had no significant effect on cortical function.

The author was not able to find any previous report of electroencephalographic studies made during carotid occlusion. In his case these showed that during temporary occlusion of the common carotid lasting almost an hour and a half no significant change in cerebral function occurred. This was supported by measurements of the strength of the hand grip made during the same interval. In such cases it cannot be said however, that a delayed hemiplegia will not follow the occlusion. An example of this occurring some twenty hours after ligation of the internal carotid has been reported by the writer in a case of fatulous carotico-cavernous aneurysm. In order, therefore to lessen the possibility of such a delayed complication it was decided to ligate the common rather than the internal carotid and thereby leave a trickle of blood through the aneurysm as in the classical operation for popliteal aneurysm performed by John Hunter on the femoral artery with the object of promoting the formation of protective laminated clots. The danger of delayed hemiplegia would appear to be greater from primary ligation of the internal carotid because having no branches this vessel when tied forms a long test tube full of blood which if it clots may by extending upward obstruct the terminal branches and thereby seriously interfere with cerebral function.

The degree of longitudinal tension in the carotid artery as evidenced by the extent of the retraction when this artery is divided (commented upon in the case recorded here) suggests that this division is advisable since it reduces the local pumping action which may liberate clot from the site of a ligature applied in continuity and thus give rise to delayed embolism.

Since reporting this case the author has operated upon 2 others in which electroencephalograms were equally helpful. In each of these as the tracing following temporary occlusion showed no significant change the common carotid was tied and divided without incident.

JOSEPH K. NARAY, M.D.

Glasser, S. T. Ligation of the Femoral Vein for Chronic Occlusive Arterial Disease: A Review of 113 Ligations. *Arch. Surg.* 1945 50: 56.

During the year of 1941 the author collaborated in the study of 20 cases of chronic occlusive arterial disease of the lower extremities in which ligation of the femoral vein was employed as the method of treatment. The encouraging results of that study demanded further evaluation of this procedure. The

present report includes 118 ligations of the femoral vein in 110 patients. The author notes that the results are far from spectacular but the value of this procedure, as judged from his experience, definitely places it in the armamentarium for the treatment of chronic occlusive arterial disease.

A discussion then follows relative to those surgical procedures which are of therapeutic value in cases of occlusive arterial disease. For the most part, these procedures actually attempt to bring about the ultimate development of collateral vessels, since this is the only means by which improvement can occur. An extensive discussion is presented of experimental and clinical reports of various workers who have studied the effects of ligation of a major vein such as the femoral.

Ligation of the femoral vein proximal to the saphenofemoral junction causes temporary edema. A small degree of this swelling may be due partly to reflex vasospasm and, when recognized, may be amenable to lumbar ganglion with procaine hydrochloride. In the experience of the author ligation immediately distal to the junction of the vena profunda with the superficial femoral vein is free from subsequent edema.

The experience with this series of cases is that there has been complete absence of pulmonary complication following ligation of the femoral veins, especially when amputation was performed subsequently.

The relief of pain following ligation of the femoral vein in the majority of cases was noted and mentioned in the preliminary report of the author. Relief of pain results not only from the increased collateral circulation with its attendant increased oxygenation of the tissues. Division of the femoral vein must necessarily include partial interruption of the sympathetic pathways and this also is a probable factor in the relief of pain.

The author discusses his technique for performing this ligation and presents an analysis of the cases which are reported. In his opinion, ligation of the femoral vein is definitely indicated for prophylaxis in chronic obstructive arterial disease—before such lesions as gangrene, ulceration, and infection present themselves. Ligation of the femoral vein is not associated with morbidity or mortality. Relief of pain was obtained in the majority of the cases. The prevention of subsequent pulmonary embolism following amputation is definite.

In order to determine indications for the procedure and a proper selection of cases, ligation of the femoral vein was performed on all patients with chronic obstructive arterial disease who consented to the operation. As a result, this series included patients whose condition was unfavorable or hopeless in view of such complications as spreading gangrene and sepsis. However, the ligation of the femoral vein was of definite value in the prevention of gangrene and the alleviation of pain. An increased collateral circulation was evidenced by increased bleeding, which was noted at amputation following ligation of

the femoral vein, and also by means of arteriography. In 6 of the patients the pulses became palpable post-operatively.
HARRIS F. THURGOOD, M.D.

Glus, J. A., McGovern, J. D., and McMurray, W. R., Jr.: Portal Vein Thrombosis following Removal of Ruptured Spleen. *Ann. Surg.* 94, 15, 100.

Thrombosis of the splenic and portal veins is a not uncommon, though often an unrecognized complication following splenectomy. It would appear that this complication is most likely to occur in splenic anemia. A case is reported in which thrombosis of the portal vein followed splenectomy for traumatic rupture of the spleen. The patient was a white male, age thirty-five who fell and struck his left costal margin against a rail five hours prior to his admission to the hospital. The past history revealed that he had experienced an attack of acute abdominal pain which had been diagnosed as gall-bladder trouble six years previously. Operation was carried out several hours after admission and the spleen, which had two deep lacerations on its convex surface, was removed. Postoperatively the temperature showed slight daily elevations from 1 to 2 degrees above normal until the patient was discharged from the hospital on the seventeenth day. While at home he had recurring attacks of pain localized to the left upper abdomen immediately after eating. Later the pain shifted to the right upper quadrant and slight jaundice developed. He was treated conservatively until twelve days after the onset of pain in the right upper quadrant, at which time operation was undertaken for subsiding acute cholecystitis and cholelithiasis. The gall bladder was edematous and friable, it contained stones and was surrounded by adhesions. Considerable bleeding which was difficult to control was encountered. The gall bladder was removed and a pack was left in place to control hemorrhage. The patient's condition was poor and he expired four hours later. Postmortem examination revealed a thrombus in the portal vein extending into both the right and left branches, and a thrombus in the splenic vein.

It is presumed that the thrombus formed at the point of ligation of the splenic vein became partly dislodged, entered the left main branch of the portal vein, and produced an occlusion. Retrograde propagation of a thrombus could then follow the clot finally encroaching upon the ostium of the cystic vein with obstruction to the venous return from the gall bladder. The resulting vascular stasis in this organ caused the clinical picture of acute cholecystitis. Previous disease of the biliary tract may have been a contributing factor. Death was caused by uncontrollable hemorrhage and shock during the cholecystectomy. The increased portal venous pressure and friability of the tissues made complete hemostasis unobtainable.

It is probably a good rule to delay all elective intraperitoneal operative procedures following splenectomy until adequate circulatory readjustments

have been made. Absence of the spleen may be a factor in the inadequate response of the patient to shock and hemorrhage. Prolonged fever, abdominal pain, increased leucocyte count, and increased platelets and erythrocyte sedimentation rate following splenectomy should suggest splenic and portal vein thrombosis.

JOHN L. LINDBQUIST, M.D.

BLOOD TRANSFUSION

Popper H., Volk, B. W. Meyer K. A. Kozoll, D. D. and Steigmann F.: Evaluation of Gelatin and Pectin Solutions as Substitutes for Plasma in the Treatment of Shock: Histological Changes Produced in Human Being. *Arch. Surg.* 1945, 50: 34.

Experiences with the administration of gelatin and pectin solutions, which were used as substitutes for plasma in the treatment of shock, to a series of 317 patients in shock and not in shock were compared. The two solutions produce an equal degree of hemodilution, which levels off with administration of higher doses of both solutions. The leveling off is more pronounced in patients with anemia and hypoproteinemia. The hypothesis is suggested that the hemodilution is started by the macromolecular solution, but is maintained by other substances, possibly labile plasma proteins.

Gelatin and pectin solutions produce an equal rise in the sedimentation rate, which is considered an index of hematological changes. The significant difference between the two solutions lies in the fact that gelatin produces less change in the tissues whereas, after administration of amounts of pectin in excess of those used for patients in shock, splenomegaly and deposition of a peculiar material in various organs may be observed. This material is selectively stained by ruthenium red, a dye used for staining pectin. It is found in phagocytic cells, capillaries, tissue spaces, and infiltrating reticulum fibers in the spleen, kidneys, liver, and lungs. It resembles deposits of amyloid, and causes a reaction of the reticuloendothelial cells. A similar picture was produced in animals by the administration of large amounts of pectin. The clinical significance of these changes is unknown.

Since the beneficial effects of gelatin and pectin appear equal, gelatin appears preferable to pectin in the form used on the basis of the changes in the tissues.

SAMUEL KAMIN, M.D.

RETICULOENDOTHELIAL SYSTEM

Mazel, M. S.: Traumatic Rupture of the Spleen. *J. Pediat.*, S. Louis, 1945 26: 82.

An analysis of 3 cases of traumatic rupture of the spleen in children revealed a history of a fall or injury to the left upper quadrant of the abdomen or lower chest with signs of internal hemorrhage and abdominal rigidity and without external signs of injury to the chest or abdomen.

The reduction of the red blood-cell count and of the percentage of hemoglobin was not pronounced a short period after the occurrence of the splenic rupture.

Roentgen examination did not show fracture of the ribs, due to the resilience of the ribs in young children.

Shock and internal hemorrhage were treated by transfusions of whole blood before and after operation. In 1 child a single rupture of the spleen was approximated with interrupted mattress sutures and continuous sutures of the capsule. Multiple injuries of the spleen necessitated splenectomy in other children.

ERNEST E. ARNHEIM, M.D.

O'Neill J. F. and Rousseau J. P.: Roentgenological Examination of the Abdomen as an Aid in the Early Diagnosis of Splenic Injury. *Ann. Surg.* 1945 122: 111.

A valuable roentgenographic diagnostic sign of splenic injury following abdominal trauma is presented. It is attributed to Solis-Cohen and Levine and is substantiated by the authors in the present article.

In splenic hemorrhage of traumatic origin the shadow of the spleen is absent and the stomach is dilated with serration of its greater curvature. The cause of the serration remains unproved. These changes are not encountered in splenomegaly or after splenectomy.

The authors present 2 verified cases of splenic injury, one with massive hemorrhage and one with moderate bleeding, which are compared with an extensive injury of the left kidney, in order to evaluate the reliability of the roentgen findings.

Conclusions from this article corroborate the presence of a gas-containing stomach with a serrated greater curvature (as demonstrated on a plain abdominal film) in either a small or large hemorrhage of the spleen.

R. A. BERGER, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Tunbridge, R. E.: Cause, Effect and Treatment of Air Blast Injuries. *War Med.*, Chic., 1945, 7: 3.

The increased use of high explosives in modern warfare has been accompanied by recorded cases of injury attributed to the effects of air blast. In a particular incident it may prove difficult to obtain an accurate history of the event, and without this it is often impossible to ascertain the exact cause of the injury as different factors may produce similar pathological changes.

The pathological findings in cases of blast injury are (a) hemorrhage resulting from rupture of the capillaries and smaller vessels, more especially those of the ear, chest, and abdomen (b) rupture of organs, pulmonary alveoli, abdominal viscera, and the aorta and (c) cerebral damage.

The finding of bilateral pulmonary hemorrhages is not, however pathognomonic of blast injury and has been described in compression asphyxia, asphyxia, carbon monoxide poisoning, and in pulmonary fat embolism.

Injuries due to air blast are best subdivided into 3 groups: mild, moderate, and severe.

The mild injuries are readily overlooked, as the symptoms are not severe. There may be tightness of the chest, pain in the wall under the sternum or of the chest, irritable and paroxysmal cough, and slight deafness. In fact, the symptoms may appear to be so out of keeping with the general well-being of the patient as to lead to their being considered psychosomatic manifestations. The later differential diagnosis provides the only clinical problem. Treatment consists of rest, mild sedation, and reassurance. Recovery is complete within fourteen days.

The moderate injuries are frequently accompanied by other injuries, and the visual evidence of wounds often leads to the overlooking of injuries due to air blast. In the author's opinion, associated surgical conditions should be treated on their merits, and operation or blood transfusion should not be withheld on account of the presence of blast injuries. The prognosis of severe wounds associated with blast injury is worse than that of wounds not so complicated, but treatment, viz., rest and oxygen, is unaffected. If pyrexia develops after a period of from thirty-six to forty-eight hours, chemotherapy should be begun because of the likelihood of infection of the hemorrhagic areas.

The severe injuries present no problem because the patient rapidly loses consciousness and usually dies within twelve hours. Temporary relief is sometimes afforded by venesection, but morphine is the chief therapeutic weapon.

Air blast is an undoubted cause of death and is a complicating factor when associated with other injuries. The sequelae from air blast are few: deafness

and postconcussive syndromes. The pulmonary lesions in persons with nonfatal injury unless secondarily infected, resolve completely. The minor degrees of injury are often overlooked, and the patients are incorrectly reported as suffering from psychosomatic disease.

JOHN E. KIRKPATRICK, M.D.

Berk, J. E. and Frediani, A. W.: The Peptic Ulcer Problem in the Army. *Gastroenterology* 1944, 4: 415.

Peptic ulcer has proved to be surprisingly prevalent among military personnel and is responsible for the loss of many manpower hours. Of 841 enlisted personnel admitted to the Gastrointestinal Section of the Tilton General Hospital, Fort Dix, New Jersey 340 or 40.4 per cent, of the patients proved to have peptic ulcer. This figure does not indicate the incidence of peptic ulcer in the armed forces at large, since this installation receives a selected group of cases. Approximately 74 per cent of the inductees in this series presented symptoms indicating the existence of ulcer prior to induction. The average length of service by the inductees prior to the first hospitalization in the Army averaged only seven and one half months. The average age of these patients was twenty-nine and one half years. In 309 cases with accurate records, 310 ulcers were found, of which 303 were duodenal, 6 gastric, and 1 jejunal. Duodenal ulcer therefore, constituted 98.7 per cent of all the ulcers, with a ratio of duodenal to gastric ulcer of 50 to 1. Atypical ulcer histories were obtained particularly from younger persons whose symptoms were of short duration. It was necessary to resort to antacids for the relief of pain in only 18 per cent of the patients. Psychosomatic factors are outstanding in military personnel with ulcers. The influence of anxiety, tension, and emotional unrest is unmistakable. There is a greater tendency toward lower levels of gastric acidity in young soldiers with ulcer than in comparable groups of older patients. This suggests that with repeated recurrences and with chronicity the gastric acidity in ulcer patients rises.

Complicating features, either in the past history or at the time of admission were hemorrhage in 17.7 per cent of 225 cases in this series, perforation in 7.6 per cent and pyloric obstruction in 3.1 per cent. It was found necessary to operate on only 3 of 340 men with peptic ulcer: on 1 because of an acute perforation, on 1 because of posterior penetration with intractable pain, and on the third because of a large gastric ulcer which failed to heal completely on a medical regimen. The authors believe that the promiscuous employment of gastric resection or other types of operative procedure in military personnel with uncomplicated ulcer merely in the hope that it will render them fit for duty is unwise.

The prevalence of peptic ulcer in the Army is largely a reflection of the unsuspected frequency of the disorder in the adult population. Although they cannot prove it the authors believe that active military service and all it connotes is influential in the causation of ulcer. They are sure that psychogenic factors connected with warfare have an influence on the clinical behavior of soldiers with ulcer. Many soldiers with ulcer tend either consciously or unconsciously to exploit their defect. In general soldiers with peptic ulcer fare poorly in the Army. For these reasons, it is the policy to separate from the service all soldiers with ulcer unless their skill, capabilities or experience outweigh the risk of their retention in the service. JOHN L. LINGGERT, M.D.

Oldfield, M. C.: Some Experience of Reparative Surgery in the Middle East. *Brit. J. Surg.* 1944, 32: 237

A preliminary review of the 1,300 cases treated by a maxillofacial unit in the Middle East during a period of two years is presented and a short survey of the methods used for the treatment of the commoner types of injury is given. Some impressions of the treatment of 195 cases of severe burns are given. The back of the trunk was involved in all of the 4 patients who died from the effects of burns. A short description is given of some of the complications that have occurred. The importance of air evacuation, burn centers, external pin fixation for certain facial fractures and rigid dressing technique is emphasized. LOUIS T. BYARS, M.D.

Bosworth, B. M.: Treatment of Fractures in the Combat Area. *Am. J. Surg.* 1945, 67: 342

Fracture at the front presents peculiar problems. Early and safe transportation is a prime consideration. Treatment must be designed for the comfort of the patient and the convenience of the medical personnel. Multiple injuries complicate the treatment. Treatment which is considered the best for fractures must often be altered. Lack of equipment is a very real factor in combat areas and those who are ingenious at improvisations will have the most successful results.

A major complication of war fractures of the extremities which the author encountered occasionally was tamponade of the circulation due to an unsuspected hemorrhage beneath the deep fascia. In many cases the bone or bones were terribly shattered and quite often there was a massive loss of soft tissues as well. All casts applied in this area were padded and then they were split or bivalved throughout their length. The separation must go through all of the dressings and bandages right down to the skin itself. The Tobruk splint for fractures of the lower extremities is described and illustrated but the author prefers a well applied spica cast.

Nerve injuries are common and are a serious complication for war fractures. The possibility of their presence must be kept in mind when the patient is prepared for primary surgery. In the combat area

open reduction of simple fractures is not permitted but the treatment of compound fractures is left pretty much up to the individual surgeon. When some form of skeletal fixation was imperative the author preferred plates of vitallium or stainless steel to the Roger Anderson and similar pin transfixion methods as he considered them to be much quicker surer and simpler. Sodium pentothal was given frequently by the intravenous method in the treatment of major fractures in the combat area.

EMIL C. ROBITSEK, M.D.

Longland, C. F. and Kessel, L.: Surgery in an Airborne Division. *Brit. J. Surg.* 1944, 32: 275

This communication gives an account of the present surgical service in a British Airborne Division and the history of its development. The general difficulties of such a service are that asepsis and mud may have to be roommates, clean areas must be guarded from the inroads of unfavorable surroundings, slender resources must be carefully husbanded, technique must be kept simple while principles are obeyed, nursing is beset with difficulties and real comfort is almost out of reach. In addition there are problems peculiar to the service.

1. Though long range mobility is one of their characteristics, once on the ground airborne troops are relatively immobile. This favors the use of operating centers which are necessarily static affairs once established.

2. Because of the lack of motor transport and the limited loads which aircraft can carry the amount of equipment these troops command is strictly limited. This affects the choice and packing of equipment. Other factors beside total weight must be considered. Loads must be designed so that they can be carried by one man across rough country on foot and these loads must fit into the containers in which equipment is carried by the aircraft. There must also be sufficient duplication of essential items to minimize the effects of loss of some loads.

3. In their most typical type of operation airborne troops fight inside enemy territory and have no rearward ground communications. This means that evacuation of casualties to rearward hospitals is impossible for some time and surgery must be provided by the medical unit concerned. Adequate nursing is essential to secure good results from the surgery and until the airborne troops join up with the ground troops the wounded accumulate in the dressing station. It may be impossible to place the operating center out of range of even the lighter weapons, but this disadvantage can be reduced if the site is carefully chosen.

Careful planning of the entire airborne operation and the co-ordination of the surgical team in the plan is essential. The surgical teams generally consist of a surgeon and five orderlies with another medical or dental officer attached as anesthetist, and as a rule two such teams work in conjunction. The teams require the help of men assigned to other duties in the main dressing station in the handling

of their equipment. After the landing the medical personnel assist those injured in the landing, and the surgical teams take no special part in dealing with these casualties. By the time the operating center is ready to function the teams will have done a considerable amount of physical work with loss of much sleep so that if conditions permit, short initial shifts are arranged for the teams.

The aim of the surgical methods is to provide the full recognized forward surgical treatment for all types of casualties, such surgery being directed toward making the patient safe and comfortable for the journey to base hospitals and giving the wounded tissues the best chance of rapid and complete healing. Such work differs little from that of the ground field surgical units. The delay in evacuations modifies the treatment to be adopted in a few special types of wounds ordinarily best sent back to specialist units, notably the penetrating head injury. Jaconet is used instead of linen and the "two-bench circuit" method of providing instrument sets for successive cases has proved satisfactory. Lighting is provided by paraffin pressure lamps with incandescent mantles, by electric head lamps, and by accumulator-operated spot lamps on stands. Penitohal-sodium anesthesia is most suitable for air borne work because of its facility of administration without bulky equipment. Ether is dangerous in the presence of naked flames and has been abandoned in favor of chloroform, which has the further advantage of being less bulky. Plaster of Paris, because of its weight and bulk, is not ideal for splinting, and it is difficult to supply sufficient quantities of this essential material. The casts used are based on three standard patterns for each limb: these are the "box" plaster, the full arm plaster and a roller splint to hold wrist, hand and digits in the position of function for the upper limb; the simplified "Tobruk" plaster for the full leg plaster and the lower leg plaster for the lower limb. Transfusion fluids are also limited because of weight and bulk. Facilities for postoperative nursing, particularly for abdominal cases, are limited. In spite of all the difficulties involved it is now possible to give isolated airborne troops the benefit of early wound surgery.

JOHN L. LINDQUIST M.D.

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

Cayford, E. H., and Pretty H. G.: Refrigeration Anesthesia and Evaluation of Amputation Sites by Arteriogram. *Ann. Surg.* 1945 21 57

Cayford and Pretty discuss the use of lowered temperatures in limb amputations of 22 patients. In nearly every instance the patient was a grave operative risk and some of the patients could not have been treated surgically were it not for this method of anesthesia. There were 4 deaths, 3 of which were due to gas gangrene.

Refrigeration anesthesia cools and numbs the tissue cells en masse. It is, therefore, a general tissue

depressant without any particular selective action on the nerve trunks. Refrigeration produces first of all, a vasoconstriction, and later a vasodilatation, this reduces edema and minimizes transudation of tissue fluids which renders the tissues firm. Shortly after refrigeration commences there is a mild analgesia over the once painful extremity. The patient, relieved of his agonizing pain may now enjoy a substantial meal before going to the operating room, or immediately afterward. There is no shock whatever to the procedure, as determined by the ordinary signs and symptoms or by the Scudder estimation. There is no real necessity of a sedative, although in many nervous people a sedative is probably advisable. The anesthesia is adequate and will last about one hour; this allows the surgeon to carry out any type of amputation procedure desired. The sawing of the bone sometimes disturbs the patient, but he will generally admit there is no pain. Severing of the large nerve trunks is quite painless but the nerves cannot be pulled down for higher section without some pain. To obviate this discomfort, it is simple to separate the muscle fibers upward an inch or so; the nerve can then be cut off above the line of amputation. Novocaine and alcohol, or novocaine alone can be injected into the nerve to avoid the painful neuroma later.

The tourniquet was dispensed with in 18 of the 22 cases, and the early and uneventful healing of the stump wounds is attributed to this fact.

A modification of the Allen technique was employed. Usually a mild sedative is given before immersion of the limb in the ice. The temperature at the skin surface is reduced to and maintained at 5° C. If a tourniquet is to be used it is applied one hour after refrigeration commences. During refrigeration the patient may be given coffee or whisky, or a regular meal. Without the tourniquet the refrigeration required is about one hour more at each site, but it may go on indefinitely without harm.

The amputation site is undoubtedly going farther down the limb. This is attributed not only to refrigeration without the tourniquet and to the improved metabolic condition of the tissues, but also to the use of arteriograms. Arteriography is a comparatively new field but it will undoubtedly offer a great contribution toward the establishment of the proper site for amputation and go hand in hand with refrigeration in the conservation of limb length and lives. It makes visible the collateral circulation which is not determined by means of skin temperatures or oscilometric readings. Furthermore, it determines the exact patency of the main vessel at a higher level than is anticipated by any other tests and eliminates any element of doubt regarding the site of amputation.

STEPHEN A. ZILMAN, M.D.

Pritchard, J. E.: The Biopsy as an Accurate Guide to the Decision of Early Skin Grafting. *Ann. Surg.* 1945 1 64.

When a burn wound requires skin grafting it is desirable that it be done as early as possible. Therefore, it is important to have some means of determin-

ing whether the wound can be expected to heal spontaneously and satisfactorily or whether this cannot be expected and skin grafting is required.

The healing of a burn depends upon the viable epithelium in the burned area which is available for re-epithermization. The epidermis at the margins of the wound the surface epithelium that has escaped destruction the hair follicles, the sebaceous glands, and the sweat glands supply the material for re-epithermization. For satisfactory spontaneous healing, there is required at least a sufficient number of hair follicles and sweat glands therefore hair follicles which lie at a higher level than the sweat glands except in hairy parts, must be spared in sufficient numbers if spontaneous satisfactory healing is to be obtained. If destruction should involve most or all of the hair follicles but spare the sweat glands which lie at a deeper level spontaneous re-epithermization may still be expected but the process will be slow and it will be attended by the formation of granulation tissue which organizes into fibrous tissue, so that the remains of the viable deep layer of the fibro-elastic corium becomes overlaid by a thick layer of scar tissue covered by hyperkeratotic epidermis—an unsatisfactory result. If the destruction extends deep enough to involve the sweat glands, there will be no source of re-epithermization other than that at the margins of the wound, and this, in all but very small burned areas, is inadequate.

At the time of removal of the first dressing all questionable cases are subjected to biopsy in order to determine the expectancy of the healing of the wound. It soon became the practice to prepare rapid frozen sections of this tissue in the operating room and upon the report of the pathologist, the decision to graft or not to graft is made at once. In the biopsies the finding of destruction of the skin to a level below the hair follicles indicates that satisfactory spontaneous healing cannot be expected and that skin grafting is required.

LOUIS T. BYARS, M.D.

Jenney J. A.: Modification of the Plasma Fixation Method (Sano) of Skin Grafting by the Use of Bobbinet and a Mirror Attachment *Am J Surg* 1945 67 3

Among the difficulties encountered in the use of Padgett dermatome grafts are the removal of the graft from the dermatome, sticking of its cemented surface to adjacent surfaces, holding the graft on the recipient area, contraction of the graft, mutilation of thin grafts when they are separated from the dermatome, and interference of vision of the operator by the drum during the cutting of the graft. To avoid these difficulties, a method is proposed which involves the use of bobbinet on the drum of the dermatome and a mirror attached to the cutting arm.

A piece of washed cotton bobbinet is cut about 1 inch larger in all directions than the area of the drum of the Padgett dermatome. The drum is painted with rubber cement, allowed to dry, and the piece of bobbinet is then rolled onto the drum. Another coat

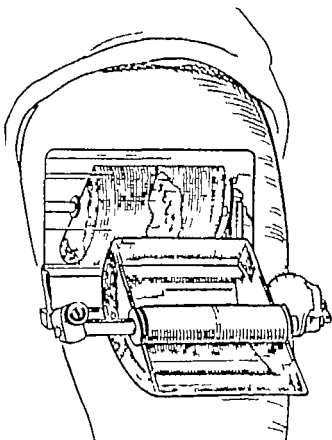


Fig. Reflection of the bobbinet and graft in the mirror (Courtesy of American Journal of Surgery)

of cement which is sufficient to saturate the bobbinet thoroughly is applied and the ends and sides of the bobbinet are pasted down. The drum may then be autoclaved or sterilized in a steam sterilizer. Adhesive qualities of the sterilized drum are tested with the surgeon's glove and if the drum is a little dry it is repainted with a thin solution of the cement.

A pattern is then made of the recipient area and it is marked out on the donor area with dye. The skin is then superficially incised with a scalpel along the line of the borders of the graft. The area within the incised line is cleaned with ether and painted with rubber cement; the area outside the incised line is powdered with talcum or sulfazaline to prevent adhesion between the rubber on the dermatome and the skin. The skin around the recipient wound is painted with rubber cement. The mirror is then attached to the instrument and the graft is cut in the usual manner (Fig. 1). The ends of the bobbinet are loosened and by gentle traction the fabric with the adherent skin is peeled off the drum. Towel is applied to the rubberized surface which was next to the drum in order to avoid adhesion to gloves.

Graft and recipient areas are treated according to the plasma fixation technique of Sano. The graft is then fitted accurately to its place in the wound being applied at one end and rolled down and the margins of the rubberized fabric are pressed into the prepared skin to which they adhere. Sutures are

placed, if needed and a pressure dressing is applied. Good results have been obtained on even surfaces with no dressings at all over the fabric, but in such cases bleb formation is more common. When the grafts have become well vascularized the bobbinet may be removed. By saturating the deeper layers of the dressing with either or cement solvent, the bobbinet can be picked off easily. In covering large granulating wounds the bobbinet held grafts may be cut into strips which are laid across the prepared base and pasted to the skin adjacent to the wounds.

The advantages of the bobbinet are that it facilitates handling of the grafts, thin grafts are not mutilated pattern grafts may be cut accurately contraction of the grafts is eliminated the grafts can be molded over forms to line cavities as in buccal ulcers, and a minimum of suturing of grafts is needed.

The mirrors are cut from large metal mirrors such as are used by photographers. They measure 7 by 3½ inches and are fixed by posts to the cutting arms of the dermatome or to the knife clip. The mirror simplifies the cutting of the graft by adding illumination of the graft, and by permitting the operator to work in a comfortable position and to view the operation of the knife at all times.

JOSEPH J. McDONALD, M.D.

Roberts, W. M. and Schaubel, H. J.: Vaseline Gauze Contact Fixation of Split Thickness (Padgett) Skin Grafts. *Am. J. Surg.* 94:5 67, 6.

To overcome the problem of fixation of split thickness grafts to the recipient area, and particularly to avoid the tedious job of suturing the grafts, the authors have sought new techniques. Fixation with strips of adhesive tape was tried and although this method was more rapid than suturing and gave a satisfactory percentage of take it was found to be time-consuming. Furthermore, the edges of the skin graft showed a tendency to curl under and the graft would retract to some degree because of its inherent elasticity.

More recently a fixation method by means of contact of the skin with vaseline gauze has been employed. Sterile vaseline gauze strips about an inch wider and longer than the graft to be taken are made up. After the graft is cut with the Padgett dermatome hemostats are clipped onto the skin graft borders, and with these as handles, the graft is placed on the vaseline, the stratum corneum layer being in contact with the vaseline gauze. Sulfathiazole powder is sprinkled on the raw surface. The hemostats are then removed from one end of the graft and a picture roller guided across the graft under constant firm pressure, removes the remaining hemostats as the roller passes them. The graft now adheres firmly to the vaseline gauze with no tendency of the skin edges to curl. In the absence of a picture roller the graft can be pressed onto the vaseline gauze with Kelly clamps. The graft is then transferred to the recipient area, and through the transparent vaseline gauze it is a simple matter to place the graft in exactly the desired position. The overlapping vaseline-

gauze borders adhere nicely to the healthy skin borders surrounding the wound and no sutures are used. A pressure dressing is then applied and held in place by a stockinette bandage. For large wounds, several drum grafts may be placed side by side on large sheets of vaseline gauze, and applied with the same technique. If small pattern grafts are needed they can be easily cut to the desired size when held by the vaseline gauze.

A series of 80 patients were treated with Padgett dermatome grafts. On 43 patients, the grafts were held in place by means of adhesive strips, and on 37 patients the grafts were held entirely by means of silk sutures. The percentage of take in both groups was satisfactory. In 12 patients, the vaseline-gauze-contact method was used with an unusually high percentage of take, i.e. above 90 per cent in all cases.

The importance of preoperative and postoperative care to maintain the patient in good general physical condition is stressed. Transfusions are recommended whenever the hemoglobin level is below 86 per cent. When donor areas are limited the authors take split thickness grafts from the same donor area several times, allowing a suitable interval of time for healing. On occasion grafts have been taken from previously grafted areas with rapid healing of both the freshly denuded area and the graft.

JOSEPH J. McDONALD, M.D.

Zintel, H. A.: Resplitting Split Thickness Grafts with the Dermatomy. A Method for Increasing the Yield of Limited Donor Sites. *Ann. Surg.* 94:5 2.

In order to cover large skin defects rapidly with split thickness grafts in patients with limited donor areas a method of resplitting Padgett skin grafts into two or three layers is presented.

The donor skin is cut as thickly as possible without interfering with regeneration of the epithelium (in adults from 0.030 to 0.038 of an inch, in children from 0.012 to 0.018 of an inch). With the graft still adherent to the dermatome drum the knife is adjusted to one half the original distance from the drum. By passing over the first quarter of an inch of skin before the blade is adjusted, rolling or separation of the leading edge of the skin is prevented then by repetition of the cutting process the graft may be split into two layers. At times it is possible to cut a graft into three layers. Thus, the skin from a given donor area can be used to cover an area from two to three times as large.

The take of the inner layer of a "split-split" thickness graft is quite similar to the healing of a Padgett donor area, ten or twelve days being required for it to become covered by delicate epithelium. To avoid injury of the delicate new epithelial layer the primary dressing is not changed until the tenth day and the layer of gauze in contact with the graft may be left until the fifteenth or sixteenth day. In 5 of 6 patients in which the "split-split" thickness grafts have been tried from 90 to 100 per cent of

the grafts remained viable. In one case in which an ordinary Padgett split thickness graft was unsuccessful, split-split thickness grafts were also unsuccessful.

JOSEPH J. McDONALD, M.D.

Clute, H. M. Kenney F. R. and Hamilton, B. E.: The Management of Postoperative Complications in Thyroid Surgery *Surgery* 1944, 16 739.

Oxygen is given to many patients after thyroid surgery for some hours after operation especially if they are toxic. Glucose in distilled water or in saline solution is given intravenously. Lugol's solution may be added to the intravenous solution. Nausea and vomiting which are usually due to the preoperative and postoperative medication and the anesthetic are readily managed by replacing intravenously the fluids and salts that have been lost. Nausea and vomiting are not infrequently related to the use of morphine and cease when this drug is discontinued.

Postoperative hemorrhage is a rare occurrence but when it does occur it may develop at catastrophic speed. When such a hemorrhage occurs the wound must be widely opened in the patient's room. Large gauze packs should then be placed over the wound and the patient returned to the operating room. The bleeding vessel should then be ligated. Severe hemorrhage is usually from the superior or inferior thyroid artery and if no bleeding point can be found then both vessels should be ligated.

The authors remove all skin sutures twenty four hours after operation. This greatly improves the scars. No wounds have separated following this procedure. Should serum collect under the skin it is aspirated. Should brawny edema of the skin flaps develop it should clear up in a few days. Hot poultices or ice bags may be applied for comfort.

A rare complication is an infection extending into the superior mediastinum. This is most apt to occur after the removal of a substernal goiter. It should be suspected if there is a rising pulse and a moderate fever the pulse being proportionately much higher than the fever when there is toxicity of the patient. A ray examination should show typical widening of the mediastinum. Immediate reoperation is indicated to cut the prethyroid muscles transversely and drain the mediastinum.

Tracheitis may be relieved by steam inhalations. Marked stridor, cough, trouble in swallowing and even regurgitation of liquids through the mouth or nose are most unusual. They are probably due to injury to (1) the superior or inferior laryngeal nerve, (2) the fine muscles of the neck, or (3) an actual spasm of the tracheal muscles. Temporary relief may be gained by the use of oxygen or oxygen and helium. If marked swelling is present, the wound must be widely opened and preparations made for tracheotomy. The tendency in the presence of marked stridor is to delay tracheotomy too long.

Injury to one recurrent laryngeal nerve may occur with no accompanying symptoms. After operation the patient's voice may be affected particularly

as to tone and volume, this may be a transient or permanent change. No special treatment is indicated. Bilateral injury to this nerve is most serious and may be fatal. Should this complication occur examination of the larynx makes the diagnosis readily apparent. The seriousness of this complication may not become apparent until the patient is up and about, when with increased exercise breathing becomes more difficult and a great increase in stridor occurs. In such cases eight or ten months should elapse before any radical treatment is instituted as one cord may regain its motility. Submucous resection of the cords or the transplantation of the omohyoid muscle to the base of one arytenoid cartilage and reconstruction of the larynx should be considered.

Postoperative thyroid storms are far less frequent and much less severe than in the past. In serious postoperative thyroid cases the patient is placed in an oxygen tent at once and oxygen continued for hours or days as indicated. Intravenous instillations of 5 per cent glucose in physiological saline solution alternated with 5 per cent glucose in distilled water are given so that the urinary output is brought to 1000 or 1500 cc. per day. Ten drops of Lugol's solution are added to each intravenous infusion until 30 drops per twenty four hours are given.

Auricular fibrillation is no cause for alarm. The authors use digitalis to control the heart rate in these cases. Recently they have used lanatoside C intravenously. Tetany is treated by giving calcium lactate intravenously. EARL O. LATIMER, M.D.

ANTISEPTIC SURGERY TREATMENT OF WOUNDS AND INFECTIONS

Patrick, W.: Wound Treatment by Delayed Suture *Brit. M. J.*, 1944, 2 788.

The initial operative treatment of soft tissue wounds in conjunction with sulfonamide or penicillin therapy and early secondary suture along with the technique of penicillin administration are intended to prevent or minimize infection as well as to encourage early healing. In spite of these efforts in the forward areas, very many granulating wounds, some of considerable size, still reach the base hospitals with infection well established. Some time has usually elapsed since the injury, and these wounds are regarded as old but healing by granulation tissue should not be accepted as the inevitable outcome. Part of our obligation is to obtain a soundly healed wound in the shortest time. This infected granulating type of wound takes weeks and some times months to heal if left to granulate, nor is it wise to attempt a secondary suture. These wounds can be very easily treated by the "cure of excision and suture, as opposed to the prevention of the early treatment and it is on that account that this method has been investigated.

A number of granulating wounds, practically all infected were submitted to a strict uniform opera-

tive detail described by the author. In order not to obscure the effectiveness of the operative part of the technique, no particular attention was paid in any way to preoperative control of infection. No case was especially selected. A wound was decided, crudely perhaps, to be suitable for suture simply when it looked clean there was no bacteriological control. The bacteriostatic agents employed were sulfanilamide, sulfathiazole, and penicillin (which was probably some months old its strength was 5,000 units per gram) three separate series of cases were treated and each was given a different powder. The success of the technique was judged entirely by the healing of the wound and any degree of infection which may have developed. It has been estimated on a percentage basis for tabulation as follows:

	Pw cent
Completely healed on tenth day without infection and remained healed subsequently	100
1. Very minor stitch-hole infection; wound a little "grumbly" but dry and healed at second dressing on sixteenth day	90
2. Definite stitch-hole infection with some pus or discharge perhaps slight wound-gap in places, but dry and healed on twenty-second day	80
3. Infection prolonged after twenty-second day some definite breakdown of suture line likely to be some granulation	70
4. Failures and generally poor or worse results than in pre-tious group	below 70

Series 1 consisted of 10 cases. The bacteriostatic powder used was a mixture of penicillin and sulfanilamide in a proportion of 1 to 10. The wounds in this series were on the whole rather above the average size and the time interval between wounding and suturing was relatively long. The results were quite satisfactory 8 wounds of 10 (80 per cent) being completely healed within three weeks. The penicillin-sulfanilamide mixture was considered to be too strong and the series was discontinued after 10 cases.

Series 2 consisted of 28 cases. Sulfathiazole was substituted for sulfanilamide and the strength of the mixture decreased to from 1 to 20. The wounds were somewhat smaller than in the first group and the time interval was, if anything, some days shorter except in a few cases in which the delay before operating was due to a heavily infected wound. There was an improvement in the results over those of the first group some 25 cases of 28 (practically 90 per cent) being completely healed in three weeks, although 7 of these were "second-class" results. Five transverse wounds, 4 of them in the thigh, were healed completely on the tenth day.

Series 3 consisted of 18 cases. Penicillin was discarded and sulfanilamide used alone. The wounds in this group were smaller the time interval shorter, and the bacteriostatic agent weaker than in any of the other groups. The results were generally somewhat inferior only 14 wounds of 18 being healed within three weeks, 9 with "second-class" results.

The main result of the investigation is that 47 wounds of 56 (84 per cent) were healed completely

within three weeks of suturing and that 23 of these 47 wounds (nearly 60 per cent) were healed by first intention on the tenth day. The object of changing a granulating wound into a healed wound in a short time has thus been attained. Further in the failures no wound was rendered worse by the operation, and even the "poor" results were an improvement on the original condition of the wound. The combination of a strong bacteriostatic powder and a longer time interval before suture in series 1 and 2 has produced better results than the weaker powder and shorter time interval of series 3 in which, however, there have been more "second-class" results. This would suggest, in this type of wound, that there may be some definite advantage in delaying operation for some time, apart altogether from the degree of infection which may be present, although the poorer results may be due entirely to the weaker bacteriostatic powder employed. These powders can be used in many varieties of strength and mixtures and in conjunction with variations in the time-interval factor.

The causative missile has been mainly the high-explosive shell or mortar shell the nature of the missile causing the wound has had no obvious effect on healing, nor has the healing process been obviously affected by the location, situation, or direction of the wound. The direction of the new wound should be longitudinal. Longitudinal wounds are more easily repaired, and should do better mechanically than those which are transverse both to the axis of the limb and to the line of muscular contraction. Wounds are mostly opened up in a longitudinal direction at the time of the original operation so that the direction of the new wound in most cases is predetermined. The surface area of the granulating wound to be excised is of no consequence provided the skin edges after excision can be approximated for suturing without tension. The depth of the granulating wound has some bearing on ultimate healing, as this may harbor a potential source of infection. The healing of 47 of 56 wounds subjected to the treatment is a definite indication that the method of excision and suture can be applied to these infected granulating wounds with the expectation of obtaining a cure. Still better results can be obtained by the carefully planned administration of preoperative penicillin. The sulfonamides, in the presence of infection, are not strong enough to be used alone.

The advantages gained by the technique have been (1) a considerable saving in healing time, which can be estimated in days as against weeks of a granulation hill-up (2) a clean first-intention wound (3) a soft, painless, nonadherent scar and (4) a more rapid and more complete functional recovery.

CHARLES BARON, M.D.

Kerr A. B., and Werner H.: The Clinical Value of a Growth Promoting Substance in the Treatment of Indolent Wounds. *Brit J Surg* 94: 3 28

The results of a clinical trial of a tissue extract known to possess the property of stimulating growth

in tissue cultures is reported. The material used was a powdered preparation of sheep's heart as prepared by Werner and Doljanski, and designated H E P (heart-extract powder). A total of 36 cases of indolent ulcers, burns and wounds which had failed to respond to orthodox methods of treatment were treated with this substance. Of these cases 33 have fulfilled the authors' criteria of success. Only 3 failed to show an adequate response. The lesions were dressed daily or on alternate days. Treatment consisted of gentle cleansing with saline solution followed by light sprinkling of the wound with H E P. The lesion was then covered with gauze either soaked in saline solution or lightly impregnated with vaseline.

Within a week of the commencement of treatment a development of fresh pink granulations was usually to be noted on the base of the wounds. This was accompanied or immediately followed by obvious epithelial spread from the margins. Thereafter healing proceeded normally and the ultimate scars presented no unusual features.

The material was also used in preparing sites for grafting when previous skin grafts had failed to take with complete success. In several cases in which very large areas were pinch grafted H E P was applied beneath the dressings on one half of the area grafted, but no difference could be observed between the grafts on the treated and untreated areas. It is to be noted however that in these cases the dressings could not be disturbed for several days to permit repeated application of the powder. Unsuccessful attempts were made to correlate the bacteriological findings with the occurrence of nonhealing and also with the response to the powder made of heart extract.

It is concluded that growth stimulating substances are of value in the healing of wounds in man. Several incidental observations were made in this study: namely, in multiple wounds healing and non-healing tend to occur in all wounds simultaneously; also, the augmentation of the tendency to heal by growth-promoting substances may lead to an improvement in the general condition of the patient.

JOHN L. LINDQUIST, M.D.

Boston, R., and Kurman, R. Tetanus: A Report of 2 Cases Treated with Penicillin. *J. Am. Med. Ass.* 1945 127 26.

The authors present 2 cases of tetanus treated with penicillin. Each was given large doses of tetanus antitoxin and sulfadiazine. When relapses occurred penicillin therapy was instituted in heroic doses. The first patient, age twenty-two, was discharged and cured on the thirtieth hospital day, and the other, age nine, was discharged entirely cured on the twenty-fifth day after admission.

In view of the high mortality of tetanus even in cases which have been treated with large doses of tetanus antitoxin the addition of the penicillin apparently a life-saving measure.

CHARLES BARON, M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Tanner, N. C.: A Critique of Gastroscopy. *Brit. M. J.* 1944 2 849.

From the beginning of the war until December 1943, 2,200 gastroscopic examinations were done on 1,738 patients. Four hundred and seventy repeat examinations were done mainly to follow the progress of ulcer while under medical treatment to confirm healing to observe relapses and less frequently to confirm doubtful diagnoses, particularly those of cancer. Examination of the 1,738 patients revealed 589 gastric ulcer lesions, 39 gastric and duodenal ulcers, 77 postoperative ulcers, 101 gastric cancers, 267 cases of gastritis, 296 cases of duodenal ulcer, and 262 cases of functional or extragastric dyspepsia with a normal stomach. The remainder were varied pathological entities and unsuccessful or incomplete examinations.

In this clinic the main usage of the gastroscopy was for diagnosis and observation of gastric ulcer. Of the 631 gastric ulcers, 159 were diagnosed solely by gastroscopy as they apparently had normal x-ray findings. There are several reasons for the difficulty in diagnosis of many of the gastric ulcers. For example, an acute ulcer may have been too shallow to retain barium or after a hemorrhage its base may be filled with blood-clot which prevents the entry of barium to the crater. Or there might have been considerable delay after hemorrhage in x-ray examination of the patients, during which time the ulcer could heal and the scarring be missed roentgenologically. In cases of this type gastroscopy may show a well marked crater, the cause of the bleeding. At other times large ulcers particularly in the neighborhood of the angulus, may be missed roentgenologically but are readily visualized with the gastroscopy. In addition, gastric endoscopy sheds a good deal of light on the progress of the ulcer during healing. It is undoubtedly the most reliable guide in assessing the progress or failure of healing under medical regimes.

The first impression was that most gastric ulcers heal when treated in the hospital whether the patients are on ulcer diet, alkalization or just taking the normal hospital dietary with no drugs.

Gastroscopy is not indicated when it is possible to visualize the duodenal ulcer with x-rays and the diagnosis is consistent with the symptoms. But when roentgenography is uncertain or the symptoms are suggestive of a gastric lesion, particularly in the fifth decade of life, gastroscopy may be of some help. Thirty-nine of the patients with duodenal ulcer in this series also had a gastric ulcer and cancer was also seen on 2 occasions when duodenal ulcer alone was suspected roentgenologically. The author agrees that even direct visualization of an excised ulcer of the stomach may not abide the truth as to its innocence or malignancy. Nevertheless one is rarely in doubt after gastroscopic visualization, because vitality appears to accentuate the differences and where such doubt exists a second inspection

after ten days of medical treatment usually gives the clue. Certainly it is well worth while to gastroscopically examine every ulcer that is not healing rapidly under medical management." Superficial types of cancer may be missed roentgenologically and in this series there were 13 cases of cancer which had been considered benign or had not even been diagnosed roentgenologically.

There were 77 stomachs examined after operation, some merely for the purpose of investigation rather than for the suspicion of recurring ulcer. Inasmuch as this field is notably difficult for roentgenology gastroscopy is always advisable if anastomotic ulceration is suspected. In the absence of a gastrojejunal ulcer the stoma usually remains open. However if there is an ulcer on the jejunal side edema and spasm of the stoma may obscure the lesion. If there is a marginal ulcer on the gastric side, it can be easily visualized.

The diagnosis of gastritis still remains difficult. It is hard to know where the normal ends and the abnormal begins. In general, the gastric mucosa may be divided into three groups. The thick, with the *arcae gastricae*, is clearly seen as well as the medium and finally there is the thin which may be so thin that the submucosal vessels may be vis-

ible through it. Of the 49 patients with gastritis and a thick mucosa, 32 had severe symptoms. In only 4 of the 155 cases with a medium mucosa, was the condition severe enough to be a likely cause of the symptomatology. Of the 63 patients with gastritis presenting a thin or atrophic mucosa, 39 had severe symptoms.

The gastroscope is therefore most useful for pre-operative investigation. It can avoid unnecessary extensive and radical gastrectomies. It may even visualize such lesions as gastric diverticulum mucosal polyp and an occasional gastric carcinoma missed by the surgeon at laparotomy.

In view of the usually direct relationship between thickness of the gastric mucosa and its acid-pepsin secretion potentialities, some help may be gained in considering whether radical surgery—gastrectomy or palliative gastrojejunostomy—may be more advisable. The patients with thick mucosa are usually more likely to experience recurrent ulceration.

It is not the purpose of the author to make comparisons between gastroscopy and roentgenology. The methods are, of course, complementary and this study is intended to show the place that gastroscopy is making for itself in medicine.

SAMUEL J. FOGELSON, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Jacobs, E. A. Culver G. J., and Koenig, E. C.:
Roentgenological Aspects of Retroperitoneal
Perforations of the Duodenum *Radiology* 1944
43 565.

Perforation of the duodenum occurs most frequently into the free abdominal cavity. The clinical signs and roentgen appearance of this are well known. Early treatment has resulted in a surprisingly low mortality.

A retroperitoneal perforation of the duodenum is encountered in some cases of peptic ulcer and especially following trauma. About 10 per cent of all ruptures of the gastrointestinal tract occur in this part of the bowel and one-third of them are located retroperitoneally as a rule in the second and third portions of the duodenum. The mortality rate continues around 90 per cent.

The clinical picture is characterized by the fact that the trauma itself which usually is of the blunt type, elicits comparatively few symptoms. Only several hours later with the advent of the effects of the extravasation have the symptoms become marked. The duodenal contents rapidly infect the surrounding structures with the result that retroperitoneal cellulitis and necrosis set in and eventually lead to generalized peritonitis.

According to Miller the findings at operation are practically pathognomonic. The extravasated blood and duodenal contents are found either in the root of the transverso mesocolon or in the root of the mesentery of the small bowel or both, and in the intervening retroperitoneal space, very often extending somewhat to the right of the kidney. The tumor usually is crepitant since it contains gas.

The roentgen diagnosis is based on the visualization of this gas which often produces a rather wide spread emphysema. It is interesting however that although retroperitoneal perforations of the duodenum have been reported in the literature scores of times and emphysema was noted (clinically at operation, or at autopsy) in approximately 80 per cent of the cases, there are only 3 instances in which the diagnosis was made by roentgen study. The authors briefly review these 3 cases and add 2 of their own.

The first of the authors' cases clinically suggested possible perforation of the ascending colon and a scout film of the abdomen taken the day after injury revealed no evidence of free air or emphysema. Autopsy showed an acute perforation of the anterior wall of the third portion of the duodenum leading directly into the root of the mesentery with the formation of a huge, fetid dissecting retroperitoneal phlegmon, but no evidence of interstitial emphysema. The second case resulted in recovery following conservative treatment, and although the diagnosis

was not proved beyond doubt the roentgen findings indicated retroperitoneal perforation of the duodenum. There was a streak of air extending along the left side of the spine through the diaphragm presumably along the great vessels to the inferior mediastinum and another streak branching off underneath the left leaf of the diaphragm apparently between the muscle and the parietal peritoneum. This appearance did not change with shift of position of the patient.

The authors include a schematic drawing showing that the extravasated material from a retroperitoneal perforation of the duodenum tends to extend along on or several of the following courses according to the location and duration of the perforation: (1) along the root of the transverse mesocolon (2) along the root of the mesentery of the small bowel (3) along both an I in the intervening space (4) over the right (rarely the left) kidney (5) downward along the root of the mesentery of the ascending colon and cerum (clinically this may simulate and occasionally has been diagnosed as appendicitis or appendicitis abcess) (6) downward along the psoas muscle to the brim of the bony pelvis or to Poupert's ligament simulating a psoas abscess and (7) along the great vessels through the diaphragm into the inferior mediastinum.

The opinion is expressed that a roentgen diagnosis of retroperitoneal perforation of the duodenum should not be difficult in most instances. Roentgenograms should be made with the patient in the supine the upright the left lateral decubitus, and the lateral positions. In case of negative findings examination may be repeated after a few hours unless immediate surgical intervention is indicated.

T. LEUCUTIA, M.D.

Habbe J. E. and Wright H. H.: A Ray Evidence of Old Forgotten or Previously Undiagnosed Fractures. *Radiology* 1944 43 531

The authors report a series of old healed fractures, involving practically every major part of the skeleton which had gone undiagnosed from a few months to a number of years. In some instances a subsequent second injury led to the discovery of the old fracture. In others routine survey examinations permitted recognition of the previously missed fracture. From the medicolegal standpoint it is important that most of these patients could not recall any injury that might have accounted for the fracture. This applies especially to certain fractures of the carpal scaphoid of the middle and lower ribs of the metatarsal and metacarpal bones, and of all the phalangeal bones. The functional recovery as a rule was excellent and later the roentgen deformities of the affected bones constituted the sole positive evidence that there was a traumatic injury. It is the authors' contention that under such circumstances

the roentgen findings must be accepted at their full value, even in apparent contradiction to the history of the patient. The fractures may be placed in three categories (1) undiagnosed, (2) untreated or at least inadequately and unorthodoxically treated and (3) ultimately forgotten.

The cases described include unusual fractures of the seventh to twelfth ribs of the manubrium sternal of the carpal scaphoid of the distal radius and ulnar styloid of the metatarsals, metacarpals, and phalanges of the calcaneus of the vertebral bodies of any location of the bones of the pelvic girdle and of the zygomatic arch—20 cases in all.

Numerous very instructive roentgenograms are used to illustrate the points in question. It is recommended that in all such instances roentgenograms in multiple positions be made whenever possible.

T LUCOTTA, M.D.

MISCELLANEOUS

Spear, F. G., and Tansley, K.: The Action of Neutrons on the Developing Rat Retina. *Brit. J. Radiol.* 944 17 374

The authors, in collaboration with Gluecksmann have published since 1936 a series of articles dealing with the dependence of degeneration upon mitotic activity in developing tissues exposed to small doses of x rays or gamma rays. In the present article they investigate the problem as to whether a similar effect occurs with the neutron rays. As in the previous experiments, the immature rat retina was chosen for the testing.

The irradiations were carried out in co-operation with Aebemold on the 37 inch, 80-ton cyclotron at Professor Lawrence's Laboratory in Berkeley California.

Two-day old rats were used and certain precautions were taken to insure that adequate maternal care was provided, a point of considerable importance. The whole body of the rat was exposed lots of 4 or 5 rats being placed in one "layer" in a

small cardboard box with a perforated lid and immobilized with cotton wool.

The cyclotron operated at 8 mv and from 60 to 80 μ A ion beam, the neutrons being produced by the Be-D reaction. The beam was passed through a suitable lead and water tank collimator and the radiation traveled a distance of 70 cm. to the rats. The dose was measured by a Victoreen ionization chamber and 1 n was considered to be 1 roentgen (as calibrated for x rays) although the unpublished work by Aebemold and Lawrence and a personal communication by Gray seem to indicate that 1 n probably equals from 2 to 2.5 roentgens of gamma rays.

Amounts of from 2.5 n to 60 n were administered, the exposure times varying from three-fourths minute to twenty-four minutes.

After exposure the rats were returned to their mother for from one and one half to seventy two hours and were then killed either by decapitation or by ether. The two eyes were dissected out and fixed in Zenker's solution. The corresponding controls were killed at the same time. After paraffin embedding, one eye from each rat was dispatched to England. The other eye was analyzed at Berkeley.

The biological response was measured quantitatively in terms of the mitotic and degenerate cell counts. The results obtained were arranged tabularly and plotted in graphs. They were then compared with the data from the former gamma ray experiments.

In a general way it was noted that neutron radiation produced an initial fall in mitosis, which was followed by a return to a cell division characterized by a distortion of the normal phase ratio. Degenerate cells appeared between one and three hours after exposure. It is probable that the degenerate cell count is made up partly by cells killed outright and partly by injured cells which die when subsequent mitosis is attempted. This effect is similar to that observed in gamma irradiation.

T LUCOTTA, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Peterson, E. W., Bornstein, M. B. and Jasper H. H.: Effect of Morphine Sulfate on Persons Exposed to Simulated Altitude. *War Med Chic.* 1945 7 23

It is a foregone conclusion that the sick or wounded persons who are candidates for transport by air will have received or will receive morphine for the control of pain or shock. In such persons it becomes a matter of concern whether the effects of morphine on the body other than those of analgesia and sedation may seriously impair their ability to undergo air transport.

The results of this series of experiments illustrate that the pharmacodynamics of morphine in the dosage employed does not cause, in the majority of cases, a significant deviation in the oxygen saturation of arterial blood such as might be effected by the drug's action on respiration.

JOHN E. KIRKPATRICK, M.D.

Peterson, E. W., Bornstein, M. B. and Jasper H. H.: Effect of Sulfathiazole on Persons Subjected to Simulated Altitude. *War Med, Chic* 1945 7 29.

The result of this series of experiments indicates that the pharmacodynamics of sulfathiazole in full therapeutic doses did not cause any significant deviation of the oxygen saturation of the arterial blood nor was there any significant deviation to be seen in the electrical activity of the heart or the brain. It seems clear from the various objective methods that were employed in this investigation that under conditions of severe anoxia, sulfathiazole in the dosage employed failed to alter the subject's reaction to anoxia.

The experimental method employed in this study did not take into account observations on reaction time with and without sulfathiazole medication. It is noteworthy however that the subjects studied did not experience any change in the psychic manifestations of anoxia while they were saturated with the drug. It is not intended however to advance any opinion as to whether aircrew members would be fit for flying duty while taking sulfathiazole or other sulfonamide compounds.

Normal adult males receiving sulfathiazole in full therapeutic doses failed to show any significant deviation in oxygen-saturation levels in the blood in electrocardiograms, or in electroencephalograms when subjected to simulated altitudes of 20 000 feet.

Anoxia produced in the decompression chamber even at simulated altitudes of 20 000 feet failed to change in a significant manner the subjective reactions of human subjects to full therapeutic doses of sulfathiazole.

It is concluded that sulfathiazole in full therapeutic doses does not significantly alter the ability of normal persons to withstand the effects of altitude and it is concluded that the evidence does not contraindicate the use of this drug for wounded personnel who are to be transported below 10 000 feet or above 10 000 feet with supplementary oxygen.

JOHN E. KIRKPATRICK, M.D.

Robbins, S. L. and Tucker, A. W. Jr.: The Cause of Death in Diabetes. A Report of 367 Autopsied Cases. *N England J M* 1944, 231 865

The subject matter of this report is drawn from a study of 367 diabetic patients over the age of twelve they were studied at autopsy at the Mallory Institute of Pathology during the years 1932 to 1942 inclusive. For purposes of comparison, autopsies were reviewed for anatomic causes of death in approximately 2,800 consecutive patients. In 268 patients of the diabetic group adequate histological material was reviewed to evaluate the frequency of histopathological changes. The clinical impression that the diabetic patient lives as long as the non diabetic was confirmed. However the diabetic patient is more likely to encounter the hazards of coronary occlusion peripheral vascular disease infections of the extremities, and acute pyelonephritis. As regards renal changes in the diabetic group glycogen nephrosis was present in significant degree in only 42 per cent of the cases while intercapillary glomerulosclerosis was present in only 20 per cent.

WALTER H. NADLER, M.D.

GENERAL BACTERIAL, PROTOZOAN AND PARASITIC INFECTIONS

Keeney E. L., Ajello L. and Lankford E.: Studies on Common Pathogenic Fungi and on Actinomyces Bovis. In Vitro Effect of Fatty Acids. In Vitro Effect of Sulfonamides. In Vitro Effect of Penicillin. *Bull Johns Hopkins Hosp.*, 1944 75 377 393 410

The fungistatic and fungicidal effect in vitro of sodium valerate, sodium caproate, sodium caprylate, sodium caprate, and sodium undecylenate on the common pathogens and on actinomyces bovis has been studied and compared with sodium propionate. Sodium caprylate, sodium caprate, and sodium undecylenate are usually more fungistatic for the common pathogens and for actinomyces bovis than sodium propionate sodium valerate and sodium caproate. However sodium propionate inhibited the growth of trichophyton mentagrophytes microsporon felineum and histoplasma capsulatum equally as well as the longer chain, fatty acid salts, and was superior to all other preparations in its effect on blastomyces dermatitidis. Fungicidal activity is acquired as the fatty-acid chain is lengthened. Sodium

caprate and sodium undecylenate, though not strong fungicides, possess more fungicidal activity than sodium caprylate, sodium caproate, and sodium valerate. Sodium propionate does not possess fungicidal activity.

The relative toxicity of the fatty-acid salts for albino mice has been determined. The compounds enumerated in the order from lowest to highest degree of toxicity are sodium caproate, sodium valerate, sodium propionate, sodium caprylate, sodium caprate, and sodium undecylenate. The in vitro effect of sodium caprate or of sodium undecylenate on the fungi responsible for the cutaneous mycotic infections is sufficiently impressive to warrant the clinical trial of either preparation in the treatment of *trinea pedis*, *trinea cruris*, *trinea glabrata*, and *trinea capitis*. The in vitro effect of sodium caprate and of sodium undecylenate on the fungi responsible for the deep mycotic infections is impressive. However the clinical trial of these compounds in the treatment of the deep and the systemic mycotic infections and in actinomycosis should be withheld until animal experiments have been performed.

The fungistatic and fungicidal effect of sodium sulfathiazole, sodium sulfadiazine, and sodium sulfamerazine, in vitro, on the common pathogenic fungi and actinomyces *bovis* has been studied. The inhibiting effect of these sulfonamides on the growth of the fungi that produce the superficial mycotic infections, that is, trichophyton mentagrophytes, trichophyton rubrum, epidermophyton floccosum, microsporum audouinii, microsporum felineum and candida albicans, is not sufficiently impressive to warrant their use in the treatment of the skin infections that they produce. The inhibiting effect of these sulfonamides on the growth of the fungi that produce the deep and the systemic mycotic infections, that is, cryptococcus neoformans, blastomyces dermatitidis, sporotrichum schenckii, coccidioides immitis, phialophora pedrosoi, and histoplasma capsulatum, is only impressive for phialophora pedrosoi and histoplasma capsulatum, the respective causes of chromoblastomycosis and histoplasmosis. The clinical trial of sodium sulfamerazine in the treatment of chromoblastomycosis, and sodium sulfathiazole in the treatment of histoplasmosis is warranted. The inhibiting effect of these sulfonamides on the growth of actinomyces *bovis* is not spectacular and conservatism should be displayed in regard to expectancy of cure from their use in the treatment of human actinomycosis.

The fungistatic and fungicidal effect of purified penicillin, in vitro on the common pathogens and on actinomyces *bovis* has been studied. Purified penicillin in a concentration of 10 oxford units per cubic centimeter of culture media failed to inhibit the growth of trichophyton mentagrophytes, trichophyton rubrum, epidermophyton floccosum, microsporum audouinii, microsporum felineum, candida albicans, blastomyces dermatitidis, sporotrichum schenckii, cryptococcus neoformans, coccidioides immitis, phialophora pedrosoi, and histoplasma cap-

sulatum. Penicillin, in many instances, stimulated the growth of pathogenic fungi in vitro. The use of penicillin in the treatment of the superficial and the deep mycotic infections is unwarranted and contraindicated. Penicillin in a concentration of 0.01 Oxford unit per cubic centimeter of culture media inhibits and apparently kills the actinomyces *bovis*. Clinical reports on the use of penicillin in the treatment of human actinomycosis have not been sufficiently impressive to warrant unrestricted enthusiasm on the part of the clinician for this mode of therapy.

W. H. NIXON, M.D.

Todd, E. W., Turner, G. S. and Drew, L. G. W.: Temporary Character of "Fastness" of Staphylococci to Penicillin. *Brit. M. J.* 1945, 1: 11.

It is believed that micro-organisms which have been made resistant to bacteriostatic drugs or to antibiotic agents by continued subcultures in increasing quantities of the antibacterial substance will remain fast after many subcultures in ordinary laboratory media. This has been demonstrated with the micrococcus lysodeikticus made resistant to lysozyme wherein after repeated subcultures extending over nine months in ordinary culture media, the resistance was fully maintained and a *sella* pyridine-fast strain of pneumococcus Type I remained resistant after 30 subcultures in broth.

Consequently it is assumed that bacterial resistance to sulfonamides is of a permanent character. Contrariwise, it has been found that two strains of coagulase-positive staphylococci having been made penicillin "fast" by cultivation in increasing quantities of penicillin and subcultured daily in broth without penicillin showed a rapid fall in resistance to penicillin. Therefore it appears that fastness of staphylococci to penicillin is not a permanent characteristic.

STEPHEN L. ZIMMER, M.D.

DUCTLESS GLANDS

Womack, N. A.: Thyroiditis. *Surgery* 1944, 16: 774.

Thyroiditis is encountered clinically under three main types: (1) acute suppurative thyroiditis, (2) acute nonsuppurative thyroiditis, and (3) chronic degenerative thyroiditis.

Acute suppurations are of bacterial origin and are extremely uncommon. The onset is abrupt and occasionally associated with chills. Pain is the outstanding symptom. The neck is held fixed. Swallowing is painful and hoarseness may be present. Since the advent of chemotherapy acute suppuration of the thyroid gland is becoming less frequent. Should an abscess develop, surgical drainage is indicated. The surgical incision should give adequate drainage but care must be taken not to break through the inflammatory barriers of the neck more than necessary and, in particular the pathways to the mediastinum must be protected.

Nonsuppurative acute thyroiditis is seen more frequently than the suppurative type. However, since surgical interference is seldom indicated little

is known about the disease. In view of the fact that one-half of the cases give a history of recent upper respiratory tract infection and that occasionally the process goes on to suppuration it is probable that the instigating factor in the inflammation is bacterial. The onset is not so abrupt as in the suppurative type fever is slight or absent. The gland is enlarged and tender but swelling and tenderness of the adjacent tissues are not so pronounced. The lesion is usually self limited and subsides in from ten to twelve days. Chemotherapy is suggested.

Chronic degenerative thyroiditis is of two types one described by Riedel and the other by Hashimoto. The author agrees with Graham and McCulloch who believe these are separate clinical and pathological entities and thereby disagrees with Ewing who believes that they are different stages of the same disease.

The dominant lesion of Riedel's disease is fibrosis. In about one third of the reported cases this is limited to one lobe or to part of one lobe. Extra glandular fibrosis is present in later stages. The involved gland is hard and white and not appreciably enlarged although when the surrounding muscles and vessels are involved the outlines of the gland are not too distinct. The most conspicuous clinical features are related to the fibrosis. If this is mild a slightly enlarged very hard gland may be the presenting symptom. Hypofunction of the gland may be present. Invasion of the adjacent structures by fibroblasts brings on symptoms of obstruction. Compression of the jugular veins with resulting edema and pressure on the esophagus causing dysphagia are usually earlier than severe tracheal obstruction. It is often confused with cancer and microscopic examination may be necessary to establish a correct diagnosis. Treatment is entirely related to the relief or prevention of obstruction. When only one lobe is involved resection of this lobe and the isthmus is generally feasible. When the entire gland is involved, subtotal resection is usually dangerous and removal of the isthmus in order to free the trachea may be all that can be done.

The classical picture of struma lymphomatosa (Hashimoto) as generally considered presents several differences. The entire gland is usually involved. It is lobulated very thick and its surface is smooth. The only extraglandular attachments are tracheal and these are never extensive. The gross picture is easily explained when the gland is studied microscopically. The yellow trabeculated, meaty appearance of the cut surface is due to lymphoid overgrowth. Lymphoid follicles are prominent but the lymphocytes themselves as well as the follicles differ in no way from those encountered less extensively in exophthalmic goiter status lymphaticus or even Riedel's struma the chief difference appears to be a quantitative one.

The chief damage produced by struma lymphomatosa is that of obstruction and here the indication for surgical extirpation must lie.

EARL O. LATIMER, M.D.

Nussey, A. M.: The Treatment of Hyperthyroidism with Thiouracil. *Brit. M. J.* 1944, 1, 745

Thiouracil and thiouracil probably act by preventing the union of tyrosine and iodine into diiodotyrosine which is a precursor of thyroxine. Once thyroxine is present in the body thiouracil and its derivatives cannot stop its action. This would explain the lag observed in the clinical response to thiouracil and thiouracil, and is in keeping with the observation that desiccated thyroid gland is capable of counteracting these substances in experimental animals.

At present it is possible when treating patients to inadvertently exceed the optimum dose, which causes an increase in the size of the gland and a condition resembling myxedema. Other complications known at present are granulopenia, thrombocytopenia, enlargement of the lymph glands and spleen fever and skin eruptions. Thiouracil is less toxic than thiouracil.

The author reports 27 cases of thyrotoxicosis in patients treated by these drugs for periods varying from three weeks to a year. A period of from two to eleven weeks was required to obtain a satisfactory clinical response. Doses of 0.2 gm. of thiouracil were given three times daily for a period of from three to five weeks, after which the dose was gradually reduced until the lowest dosage compatible with the patient's well-being was reached.

Signs of improvement were usually apparent in from ten to fourteen days after the beginning of treatment. Severe thyrotoxicosis frequently responded as quickly as the moderate type. Restlessness was usually the first symptom to disappear and then the flushed and moist skin became paler and drier the staring expression and the shiny appearance of the eyes faded the weight increased the tremor of the fingers became less the vascularity of the gland diminished and, finally tachycardia subsided. It was in the milder cases that tachycardia persisted the longest. In nearly all of the cases the basal metabolic rate returned to normal. Exophthalmos was unaffected by the drug nor did enlargement of the thyroid diminish to any extent. Mild myxedema occurred in a few cases, but disappeared when the dosage of thiouracil was reduced.

For a maintenance dose, the patients were usually given 0.2 gm. of thiouracil twice daily for from two to four weeks after they left the hospital. Later most of them were maintained on from 0.2 to 0.1 gm. or even 0.05 gm. daily. In a few cases all medication could be stopped. In no case was there an alarming fall of the white-cell count.

The author concludes that the drug although not devoid of risks, is much safer than operation.

EARL O. LATIMER, M.D.

Cole, W. H.: Factors Influencing the Operability and Mortality Rate in Goiter. *Surgery* 1944, 16, 688.

The marked reduction in the mortality rate following thyroidectomy during the past one or two decades has been due primarily to our increased

knowledge and application of physiological principles, particularly as related to preoperative and postoperative care. Preoperative preparation is exceedingly important in patients with severely toxic goiter.

The major factors in this preparation of the patient include (1) the administration of iodine or thiouracil (2) an increased caloric intake, (3) the conservation of energy (4) the reduction of psychic trauma (5) the treatment of complicating disease and (6) miscellaneous therapy.

Appreciating that the mortality rate is greatly dependent upon preoperative treatment, the author has adopted certain prerequisites which must be met in his clinic before a patient is considered safe for bilateral thyroidectomy. These prerequisites are (1) a gain in weight, (2) a resting pulse rate below 110 (3) a basal metabolic rate below 50 (4) response to iodine or thiouracil and (5) no untreated complications. Of this group of prerequisites, gain in weight is the most important. It is an unforgivable error to subject a patient with severe toxic goiter to bilateral thyroidectomy unless he has shown a gain in weight.

Thiouracil gives promise of revolutionizing our methods of preoperative care and may make operation unnecessary in many patients. However it is doubtful if the mortality rate may be appreciably lowered in the clinics reporting the best results, largely because relatively few of the deaths encountered in such series of patients will be related to thyrotoxicosis itself.

The mortality rate in the author's series of 936 thyroidectomies was 1.06 per cent. It was lower in toxic diffuse goiter than in either of the two types of nodular goiter. Although almost one half of the deaths must be considered in the preventable class, the causes were extremely variable. Three patients died of acute heart failure, and 2 died in crisis. There was no duplication in the other causes of death. The factors (other than coincidence) which might be responsible for a lethal outcome include (1) inadequate preparation (2) wrong choice of time for operation (3) lack of appreciation of the dangers of complications (4) errors on the operating table and (5) insufficient vigil in the postoperative care.

It should be emphasized that many of the precautions described here will be of only slight importance in the great majority of patients who respond to thiouracil. However since an occasional patient will be sensitive to the drug or will not respond to it, information gained about severely toxic patients through long experience should not be cast aside.

FARL O. LATIMER, M.D.

Holmes, J. M., and Cowan, J. M.: The Meningococcal-Adrenal Syndrome; 5 Cases with 1 Recovery. *Lancet*, Lond., 1945, 248-13.

Meningococcal infections may be classified in the following main groups:

1. *Meningococcal septicemia*. (a) Acute fulminating septicemia, with extensive purpuric eruptions

and adrenal hemorrhages, death often occurring from circulatory failure a few hours after onset. (b) Chronic septicemia with intermittent pyrexia, petechiae and skin lesions resembling erythema nodosum occasionally arthritis, and a later development of meningitis.

2. *Meningitis*. Acute, subacute, and chronic.

3. *Encephalitis*. Cases in which the intracranial lesions are far in excess of the meningitic. Deep coma may be present, and the signs of meningitis may be masked. The encephalitic type of onset often accompanies the acute adrenal syndrome, the characteristic purpuric rash and circulatory failure being seen in both.

The adrenal syndrome (Waterhouse-Friderichsen) or the meningococcal adrenal syndrome is characterized by a sudden onset of a fulminating septicemia, with cyanotic pallor like the heliotrope cyanosis in influenza septicemia. Later multiple cutaneous petechiae and possibly massive purpuric hemorrhages occur. The pulse is rapid, of poor volume, and it may be almost imperceptible. The blood pressure is low. Respiration is rapid and shallow and may become of the Cheyne-Stokes type. Consciousness may be dulled. In untreated cases, death usually occurs within twenty-four hours.

The difficulty in this type of case is in making the diagnosis and in beginning treatment as early as possible. Frequent blood-pressure readings should be taken in all cases of severe meningococcal meningitis since an abnormally low blood pressure is the only reliable early sign of adrenal failure. If treatment is withheld until the characteristic cyanosis and rapid shallow respiration appear it may be too late to be effective.

The postmortem findings suggest that death is due to circulatory collapse from a severe diminution of the blood volume. Widespread edema of the lungs and the interstitial tissues was found. In 2 cases there was an enlargement of the thymus and lymphatic glands. It is suggested that this may be a factor in determining the susceptibility of the adrenal glands to infection.

Vigorous measures must be taken to combat the circulatory failure. The sulfonamide drugs alone appear to be useless. In the few recorded cases in which treatment was successful, the sulfonamide therapy was supplemented by large intravenous infusion of saline or glucose-saline solution, and injections of adrenocortical extract or dexamethasone. Plasma rather than glucose-saline transfusion may be advisable.

SAMUEL KARK, M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Herbst, P. A., and Manges, W. E.: Melanoma of the Small Intestine. *Arch. Path.*, Chlc., 94: 39-2.

The increasing number of melanomas reported, despite the merely passing comments concerning these tumors as found in the literature, induced the

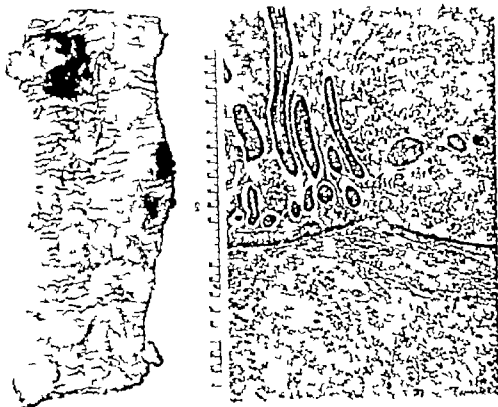


Fig. 1. a, Left, Segment of small intestine showing at least 22 blackish tumors of various shapes and sizes. b, Photomicrograph of a section of the small intestine showing tumor cells diffusely infiltrating the submucosa, breaking through the submucular mucosa, and partially replacing the vessels. Although finely granular brown pigment is abundant within the cytoplasm of the tumor cells, it cannot be seen with this magnification. (Hematoxylin and eosin)

authors to undertake this study. They have collected 25 cases, 9 primary melanomas of the small intestine and 16 of metastatic origin. The great frequency of skin melanomas was apparently not studied thoroughly enough to determine their metastases to the intestinal tract. Twelve of these melanomas were found in the last 5,000 autopsies done at the Jefferson Medical College Hospital, Philadelphia, Pennsylvania.

The authors state the purpose of this report as follows: (1) to describe 5 cases of melanoma of the small intestine; (2) to draw special attention to their accompanying clinical manifestations; and (3) to consider whether a melanoma can arise as a primary tumor of the small bowel or whether such a growth is in every case secondary to a primary focus elsewhere. A detailed report of the 5 cases is given. Figures 1 a and b are very instructive.

The knowledge gained by these studies and from the additional 5 cases (30 cases now reported) is very definite. It stresses abdominal pain with or without symptoms of intestinal obstruction, combinations of pain and fullness in the epigastrium, nausea and vomiting, anorexia, constipation or diarrhea, tarry stools, distention and tenderness of the abdomen and increased peristalsis, sometimes a liver tumor may be held responsible for the symptomatic mentioned. Sudden colicky abdominal pain followed by

nausea, vomiting and constipation may be the first and only indication for prompt operation—this is true particularly in cases of intussusception. The immediate prognosis is not entirely hopeless. 4 of the operative cases ended in recovery. One patient lived comfortably six months and then died of a lung metastasis. One patient operated upon for obstruction with resection of a tumor, was operated upon again one and one half months later for intussusception and another tumor was removed. Six months later this patient was still well. Another patient with 2 intussusceptions caused by 2 tumors, recovered but died six weeks later. The fourth patient was reported as recovered but no record of the ultimate condition was given.

Primary melanoma generally occurs in the skin or the eye. Reports of primary melanoma in the small intestine are questionable as (1) melanoblasts are found only in the skin and in mucous membranes of ectodermal origin; melanoblasts are not found in the large intestine above the mucocutaneous junction of the rectum and have not been demonstrated in the small intestine; (2) the involvement of the small bowel is the same whether or not a primary melanoma has been located elsewhere; (3) delayed metastatic growths often appear years after a mole has been removed; (4) moles that grossly and histologically appear to be benign are known to have pro-

apparent sequence is—glycogen, neutral fat anisotropic lipoids.

Xanthoma cells The stroma of 26 tumors showed this type of cell. The xanthoma cells do not appear to be neoplastic in character.

Dermoplasia. This was seen in 18 solid tumors of group 4. Interstitial fibrosis is about equally common in the more static forms of solid tumors of group 4 and is noninvasive in appearance. It distorts the arrangements of cells in the cords and islands to a marked degree.

Anaplasia This may occur in any type of tumor tissue. Isolated anaplastic areas are the most frequent source of metastases. In 18 tumors it was so extensive that analysis of their basic character was impossible.

Capsules Capsules are without significance. No conclusion can be drawn as to the liability of these tumors to spread by metastasis on the basis of the presence or absence of a capsule.

Lumens When the solidification of a papillary tumor is imperfect, lumens may be expected. They do not have regular outlines. Potential lumens are often made apparent only by hemorrhage into them or by extravasation of fluid. Thirteen tumors of groups 2 and 4 were predominantly cystic as a result of this.

Chronic inflammatory change. Extensive lymphocytic and plasma-cell infiltrations were seen in 11 tumors of group 2.

Wilms tumors occurring in adults These may show the papillary type of renal cancer. Three excellent examples were seen: papillary clear-cell cancer with rhabdomyosarcoma, group 1, 2 and 4 tumor with rhabdomyosarcoma, and group 3 cystic cancer with large quantities of adult smooth muscle.

Embryonal carcinomas. Seven solid and 2 alveolar cancers of this type occurred in the series.

Adenocarcinoma. Adenocarcinoma of the kidney does not differ greatly from that of other organs. Nine of 15 tumors thus diagnosed showed some atypical traces of tumor tissue of group 1 type. The 6 others could not be identified as renal tumor on a histological basis. The use of the term "adenocarcinoma" should be avoided elsewhere (not in group 1) in the nomenclature of renal tumors.

Opaque cell papillary tumor These are smooth cell, opaque-cell, or solid-cell cancers. The cells are larger from a broadening out of the cytoplasm which is basophilic and pale but without any granulation. The nuclei have prominent nucleoli.

SAMUEL KAHN, M.D.

EXPERIMENTAL SURGERY

Smith, L. W., and Livingston, A. E.: Wound Healing. An Experimental Study of Water-Soluble Chlorophyll Derivatives in Conjunction with Various Antibacterial Agents. *Am. J. Surg.* 1945 67 30.

A preliminary study of the water-soluble chlorophyll derivatives in various ointment bases in over

200 experimentally induced lesions in guinea pigs showed an acceleration of healing of approximately 25 per cent in time in 71 per cent of the lesions treated topically with chlorophyll as compared with those treated by the ointment base alone.

Further studies were carried out upon a series of 193 guinea pigs with bilateral symmetrical infected surgical lesions 1.0 cm. in diameter which were similarly treated by the topical application of 1 per cent chlorophyll ointment combined with various of the sulfa drugs, with penicillin and with tetrodine. Twenty four animals were used in the experiment with each antibacterial agent, being divided into three equal groups of 8 animals: one third were treated with the base alone, one third with the base plus chlorophyll alone, and the final third with base plus antibacterial agent alone.

The topical use of penicillin in strength of 250 Oxford units per gram of ointment combined with 1 per cent chlorophyll gave the most spectacular results with healing complete in ten and six tenths days as compared to fourteen and three tenths days after treatment with chlorophyll alone and fifteen days after the use of penicillin alone, an acceleration of nearly 35 per cent.

In general the sulfa compounds in combination with chlorophyll showed some acceleration of healing through their control of infection which appeared to be roughly proportional to their solubility. Experimental carboxysulfathiazole was by far the most effective of these sulfa compounds, nearly equalling penicillin in that respect. Sulfanilamide, sulfamerazine and sulfasuxidine alone in the ointment base actually caused delay in healing, and tetrodine employed in the same manner was of about the same order of effectiveness as sulfanilamide, sulfathiazole and sulfadiazine.

Experiments carried out on 8 dogs with larger wounds gave comparable results to those described in the guinea pig studies.

A small series of guinea pigs treated by chlorophyll combined with various agents as a dusting powder gave less clearly defined results, and further studies do not seem warranted. The ideal ointment base proved to be entirely satisfactory and well adapted for clinical use.

A discussion of the clinical possibilities of chlorophyll in combination with the various antibacterial agents is presented and its importance in the healing of chronic types of ulcerative lesions is stressed.

JOHN E. KIRKPATRICK, M.D.

Hartman, F. W.: Curling's Ulcer in Experimental Burns. *Ann. Surg.* 1945 121 54.

The material used as the basis for the author's article consists of 32 instances of gastric and duodenal ulceration occurring in the course of experiments on 80 dogs in which third-degree burns were produced on from 50 to 60 per cent of their bodies while the animals were under morphine and ether or morphine and chloroform anesthesia. Following the procedure, a liberal use of morphine and com-

plete dressings kept the animals comfortable, as evidenced by the fact that they were active and retained a good food intake until the terminal stages.

In the first series there were 47 third-degree burns involving from 50 to 60 per cent of the body surface, and 13 of these were associated with ulceration of the duodenum or stomach. Thirty of these burns were dressed with tanning agents, such as tannic acid, ferric chloride, and silver nitrate. In this group ulceration occurred only twice, or in 6.6 per cent, and then only in those having wet dressings. Of the 17 burns dressed with vaseline, lanolin, and scarlet r ointment, 11 or 64.7 per cent, showed ulceration. In the second series of 33 animals with burns of similar type, all were dressed with sterile vaseline, and 21 or 63.6 per cent, showed duodenal ulceration.

The gross examination of the duodenal ulcers revealed various erosions—from the most superficial mucosal lesions to penetrating invasive lesions with hemorrhage or perforated punched-out lesions with peritonitis. The inflammatory infiltration was mild (or absent) in most cases, and an acute exudate reaction was found in only 1 section. A few healed ulcer craters and large scarred areas of the duodenal wall were observed.

A comparison of the gastric contents (both after fasting and after the injection of 50 cc. of 5 per cent alcohol) of the normal dog and of the burned dog at various stages showed that both the free hydrochloric acid and the total acid were reduced sharply rather than increased. The other significant finding in the gastric contents was the blood, frequently seen as shreds and clots, and giving strongly positive chemical reactions. This, coupled with the appearance found at autopsy emphasizes the damage to the mucosa preceding ulceration or in the absence of ulceration. Hyperacidity as an explanation for Curling's ulcers is without support, according to the author's data, but normal acidity may be sufficient

to cause ulceration in the edematous, congested mucosa of these burned animals. Further it is quite possible that the usual alkalinity of the duodenal contents is reduced by mucosal damage and the developing general acidosis.

The 63 per cent incidence of Curling's ulcers in the two series of animals burned and dressed with vaseline and other bland applications, as contrasted with the 6 per cent incidence in the group burned in a similar manner and dressed with tannic acid or other tanning agents, indicates that an analysis of the two groups may suggest etiological factors. The animal whose wound is dry-tanned loses very little plasma from the body although the area beneath is always very edematous. The infection (if any) in such a wound is usually slight up until the fourth or fifth day when marginal separation of the eschar begins. The animal is comfortable and eats well after the first thirty-six to forty-eight hours. Marked acidosis rarely develops, and, barring liver necrosis, a good recovery with eventual healing of the skin defect is accomplished.

Animals treated with moist dressings of tanning agents have a course more like that of the animals dressed with bland preparations, except that necrosis and infection are somewhat reduced. With the bland dressings, the injured tissue rapidly begins to undergo autolysis. This, coupled with great and continued loss of plasma into the dressings, favors extensive infection with the various types of organisms listed. The appetite is reduced, so that despite careful feeding there is a marked weight loss, acidosis, septicemia, and coma, and convulsions are frequent.

Loss of plasma, rapid autolysis of injured tissue, with infection and acidosis are the factors which were observed in this group of animals, and these factors may logically be cited as the variables responsible for duodenal ulceration and death.

JOSEPH K. NABAT, M.D.

International Abstract of Surgery

Supplementary to
Surgery, Gynecology and Obstetrics

Volume 80
January to June, 1945

PUBLISHED BY
THE SURGICAL PUBLISHING COMPANY OF CHICAGO
54 EAST ERIE STREET CHICAGO

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